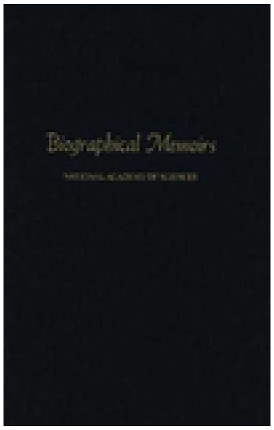

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Preface

The *Biographical Memoirs* is a series of volumes, beginning in 1877, containing the biographies of deceased members of the National Academy of Sciences and bibliographies of their published scientific contributions. The goal of the Academy is to have these memoirs serve as a contribution toward the history of American science. Each biographical essay is written by an individual familiar with the discipline and the scientific career of the deceased. These volumes, therefore, provide a record of the lives and works of some of the most distinguished leaders of American science as witnessed and interpreted by their colleagues and peers. Though the primary concern is the members' professional lives and contributions, these memoirs also include those aspects of their lives in their home, school, college, or later life that led them to their scientific career.

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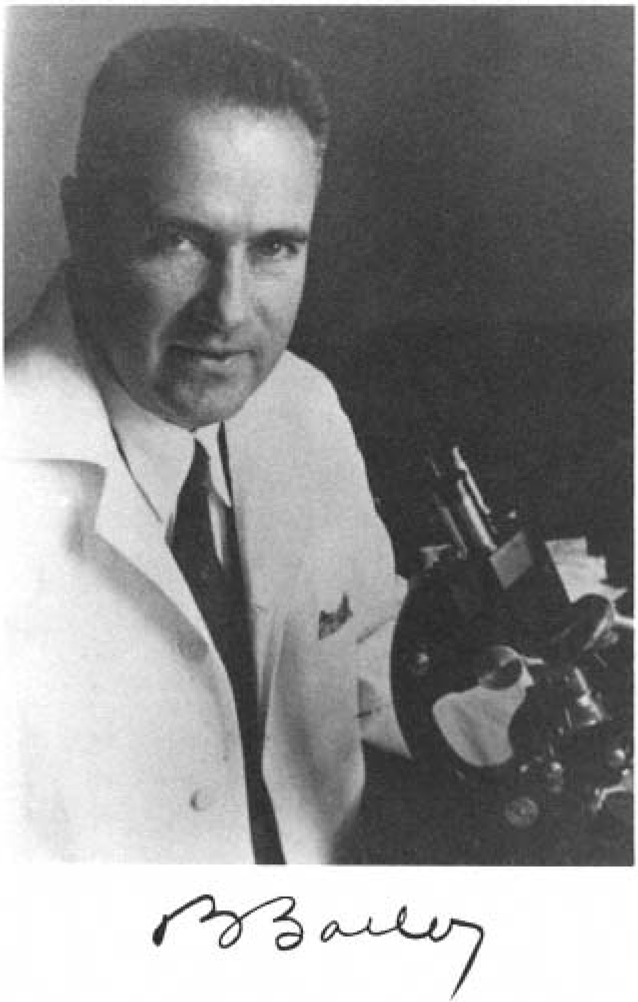

University of Illinois at Chicago Archives

Percival Bailey

May 9, 1892-August 10, 1973

By Paul C. Bucy

The barren clay hills of southern Illinois did not produce good corn or hogs, but they produced superb men. This southernmost section of Illinois is formed by the Ohio River on the southeast, by the Mississippi River on the southwest, and by an indefinite, irregular line running from a few miles north of St. Louis, Missouri, east to the Wabash River. This triangle has long been known as "Little Egypt" and appropriately has Cairo, located at the apex of the triangle and the junction of the Ohio and Mississippi rivers, as its capital.

The unproductiveness of Little Egypt led to poverty. It seems very likely that this poverty was the force that drove many intelligent young people to head North (generally to Chicago) to become distinguished judges, lawyers, scientists, and doctors. The direction of this migration was determined in considerable measure by the existence of the Illinois Central Railroad, which ran from Little Egypt directly to Chicago.

In other parts of the United States, notably in New England, similar developments have been attributed to parents' erudition and the excellence of educational opportunities. Certainly this explanation does not apply to Little Egypt. The fathers of these young men, for the most part, eked out a bare existence from the poor soil or otherwise worked daily with their hands and were often drunk. Their hard-working mothers had little time for anything but bearing children and caring for their large families.

The people of Little Egypt had migrated into southern Illinois—by way of Kentucky—from Virginia, the Carolinas, and Tennessee. Percival Bailey's forebears only partly fit the pattern. His great-grandfather, Gebhard Boehler, emigrated as a young man from Hinterstadl in Baden, Germany. He was a journeyman miller. Marrying upon his arrival in Illinois, Boehler (later changed to Bailey) added a German strain to the English, Scots, and Irish stock common to southern Illinois.

Percival Bailey's father, John Henry Bailey, never attracted his son's admiration or affection. A laborer seldom steadily employed, he drank to excess and was irresponsible. Installing his family in a one-room log hut, he took off for Cuba and the Spanish-American War.

Bailey's mother—a kindly, uneducated, hard-working woman—devoted her life to the rearing of her family. Born Mattie Orr, she married John Henry Bailey when she was seventeen years old. Percival Sylvester, her first child, was born on her eighteenth birthday, May 9, 1892. Percival had great affection for his mother, and her death in 1912, when he was nineteen years old, was a hard blow.

Dr. Bailey was never happy with either of his given names. During his early years he went by the nickname "Ves." In later life he dropped the name Sylvester and the nickname Ves altogether and preferred to be called Percy.

In 1906, when he was fourteen years old, Bailey left home after a violent quarrel with his father and went to live with his uncle, Gaphart Bailey, a farmer. His early schooling took place in a one-room country schoolhouse and was something of a "hit and miss" proposition. The school year was short, confined largely to the winter months, because children were needed to help with planting in the spring, tilling in the summer, and harvesting in the fall.

Yet many apparently unrelated developments worked to shape Bailey for the future. Hard work on his uncle's farm turned the spindly boy into a sturdy, vigorous man. It also convinced Bailey that he would not earn his livelihood with his hands. At this same time he met a remarkable character, Dr. Arsen Artin Sissakian, a country doctor he describes in a paper entitled, "Ol' Doc Artin." This philosophical Armenian and another general practitioner, Dr. George W. Barrows, who cared for Bailey's mother in her final illness, did much to turn Percy's interest toward medicine.

After completing the local country school, Bailey won a scholarship to the nearby normal school, Southern Illinois State Teachers College, now Southern Illinois University, in Carbondale. He proposed to become a country schoolteacher, a goal that was never achieved, but his experience at Carbondale was the beginning of a long series of varied influences that were to mold his future.

Throughout his life various women appeared at the appropriate time to help and guide him. First it was his mother, then Martha Buck, an Englishwoman who taught grammar and etymology at Southern Illinois. Later Ethel Terry would help him to obtain a scholarship to The University of Chicago, while Sisters Leonardo and Ethelrita at the Mercy Hospital in Chicago would protect him and teach him much about life among charity patients. Most important of all was Yevnigé Bashian, the beautiful Armenian girl that he would marry.

Martha Buck was the first person to create in Bailey the realization that he was capable of being something more than a country teacher. She stimulated and fed his ambition, and, together with another teacher, Carlos Eben Allen, guided his footsteps to The University of Chicago, which he entered on graduating from Southern Illinois Normal University in 1912. He went on to obtain a B.S. in 1914 and a Ph.D. in 1918 from The University of Chicago and an M.D. degree from Northwestern University, also in 1918.

At The University of Chicago Bailey's future began to unfold. He found himself in an academic world of which he had been totally ignorant. At The University, he came under the influence of such giants as Harvey Carr, professor of experimental psychology, who fostered in him an inquiring mind and taught him to ask, "What is wrong with this argument?" George W. Bartelmez taught him scientific method. C. Judson Herrick opened the world of neurology to him. Anton ("Ajax") J. Carlson taught him to ask, as Bailey expressed it, "Vat iss dee effidence?" Julius Grinker, not on the faculty, stimulated his interest in clinical neurology. Later, others, including Harvey Cushing, Pierre Marie, George Boris Hassin, Pierre Janet, and Gaetan Gatian de Clérambault, were also to be important in his development and training. But it was his mentors at The University of Chicago who molded Bailey into the scientist and clinician, anatomist, neurophysiologist, neuropathologist, clinical neurologist, neurological surgeon, and psychiatrist that he was to be. He became the outstanding catholic neurologist, recognized throughout the world as "Mister Neurology," a man without peer.

Bailey's Ph.D. thesis dealt with the anatomy of the brain, and he later earned money to complete his medical education teaching anatomy at Northwestern University, in Evanston. He obtained his preclinical medical education at The University of Chicago and his clinical education at Rush Medical College and at Northwestern University Medical School. During these last two clinical years, his studying was done largely on the Chicago elevated trains running between Evanston, on the north, Rush Medical College, on the west, and Northwestern University Medical School, on South Dearborn Street.

The faculties of Rush Medical College and Northwestern Medical School made little impression upon Bailey, and he never mentioned them in later years. But he often spoke with great admiration and affection of Julius Grinker, of the Postgraduate Hospital in Chicago, from whom he first learned clinical neurology. Grinker was a very able neurologist, who wrote the section on neurology in Tice's *Practice of Medicine*, a popular encyclopedic work of that time. Caustic and hypercritical, he was anything but diplomatic in his dealings with others. Yet Grinker recognized in Bailey an intelligent, inquiring young man whom he delighted to teach. Bailey in turn liked Julius Grinker and loved to learn.

After he graduated from Northwestern University in June 1918, he began his internship at the Mercy Hospital in Chicago, completed nine months later. His impressions of Mercy Hospital and its staff were for the most part unfavorable, except for two nuns Sister Leonardo and Sister Ethelrita, for whom he retained great affection and admiration. (Bailey related his experiences at the Mercy Hospital in a delightful chapter, "Sister Ethelrita," in *Up From Little Egypt*.)[1]

As he was approaching the end of his internship, Bailey wrote two letters, one to the surgeon Harvey Cushing, in Boston, and one to the psychiatrist Adolf Meyer, at Johns Hopkins. This has led to speculation that Bailey was a man who had difficulty making up his mind and could not decide whether he wanted to be a neurosurgeon or a psychiatrist. Anyone who knew Bailey well would reject this interpretation, for—even at this early date—his interest was in the nervous system rather than in any one of its disciplines. He wished to study the neurosciences and at the same time to be a clinician. He cared little whether his clinical activities were as a neurologist, a surgeon, or a psychiatrist, as was true for

[1] Percival Bailey, *Up From Little Egypt* (Chicago: The Buckskin Press, 1969) 265 pp.

the rest of his life. Cushing replied immediately, Meyer, in three months. Both accepted Bailey for training in their institutions, but Bailey had already accepted Cushing's offer and was at work in Boston when he received Meyer's letter.

Off and on, from April 1919 until July 1928, Bailey worked with Harvey Cushing at the Peter Bent Brigham Hospital in Boston. These were trying years. Bailey admired Cushing's ability as a surgeon and as a teacher of neurosurgeons. He recognized Cushing's unequaled contribution in salvaging brain surgery from a premature death, in developing that specialty, and in showing how surgical lesions of the nervous system could be diagnosed and successfully treated. Yet he had nothing but contempt for Cushing as a man. In *Up From Little Egypt* (p. 209), Bailey wrote of Cushing:

> (1) he was very artistic and had a tendency to prettify his data, (2) he had a tart tongue, (3) he had a tendency to believe anything which he imagined was true and was not too careful about the conclusiveness of his proof, (4) he had never learned to spell or write English correctly, (5) his scholarship left much to be desired.

Yet it was during his years with Cushing that Bailey became a neurosurgeon and made what was probably his greatest single contribution to neurology—his book *Tumors of the Glioma Group*, which he published with Cushing (Philadelphia: J. B. Lippincott Co., 1925, 175 pp., 108 illus.). It represents many years of hard work in which Bailey applied his knowledge of neuroanatomy and neuropathology to the definition of the microscopic nature of gliomas, their relation to the normal glial cells of the developing and adult nervous system, the clinical correlation of these tumors, and the prediction of their prognosis based on their microscopic appearance. This book completely revolutionized the understanding and diagnosis of these tumors and still influences neurological and neurosurgical thought. Its excellence and thoroughness are attested by the fact that the classification of gliomas that it proposed has changed but little over the ensuing fifty years.

Nine months after arriving in Boston, Bailey—unhappy with Cushing's behavior—returned to Chicago to work with George Boris Hassin in neuropathology at the Cook County Hospital. Hassin was one of the pioneers in neuropathology and was largely self-educated. He, too, was a difficult person, but one whose keen sense of integrity Bailey admired. In October 1920, Bailey returned to Cushing and Boston, only to leave the following year for Paris. This year in France was undoubtedly one of the happiest in Bailey's life. He always recalled it with great pleasure and frequently regaled his listeners with lively tales of his life there. At La Salpêtrière, he came under the influence of Pierre Marie, one of the greatest clinical neurologists of this century. Bailey also learned to speak French perfectly, without a trace of foreign accent, my French friends inform me.

In 1922 Bailey returned from Paris to Boston and resumed his work with Cushing for the longest continuous period he was to spend with him. While he was still a student at The University of Chicago, Bailey had developed a friendship with an Armenian theological student, Antranig Bedikian, who married Marie Bashian. At their wedding Bailey met Marie's sister, Yevnigé, who soon entrapped his heart. Cushing learned of their plans to marry.

This was in those days of long ago when medical students, interns, residents, and even young associates did not marry. Cushing feared that marriage would so divert Bailey's interests and efforts from the laboratory as to be catastrophic for his research. Learning that Yevnigé Bashian's father was dead and her two uncles, Armenian rug merchants in New York City, were the influential members of the family, he went to

New York to call on the uncles. They assumed that this distinguished surgeon from Boston had come to buy rugs. Coffee was served, and after suitable courtesies were exchanged, they got down to business. Cushing told them of the outstanding young man whose career was about to be ruined by his marriage to their niece. He could not have chosen a more disastrous means of achieving his goal. Instead of convincing the uncles to prevent the marriage, Cushing had, by his effusive description of Bailey's outstanding intelligence and great future, convinced them that here was the ideal husband for Yevnigé. He returned to Boston empty-handed—no rugs, no agreement.

Bailey's marriage further strengthened his contacts with and interests in things Armenian, begun early in life with his admiration for the southern Illinois doctor, Arsen Sissakian. Yevnigé's brother, Antranig, was to become one of his closest friends.

In 1925 the book on gliomas came off the press and Bailey had already begun work on another monograph, *Blood Vessel Tumors of the Brain*. This clinicopathological study was far ahead of its time and, as a result, never attracted great attention. In 1928 surgical techniques for treating vascular malformations were still many years away.

In 1925 Bailey returned to Paris, again following up his interest in psychiatry. On his first trip, Bailey had become acquainted with Pierre Janet, who worked at La Salpêtrière. On this second trip he worked at L'Hospice de la Ste. Anne with Gaetan Gatian de Clérambault. Janet had been influential in the development of the career of Sigmund Freud when Freud worked in Paris, but had later taken great exception to Freud's ideas, based more and more on what patients told him. Janet, wrote Bailey (*Up From Little Egypt*, p. 213), "distrusted memory and had no use for accounts of the sayings of patients unless recorded at the time." De Cléram bault, on the other hand, was a firm believer in the organic nature of psychiatric disorders: "These phenomena Clérambault believed to be due to intracellular changes in the neurones of the cerebral cortex." (p. 214)

Bailey had given evidence of his interest in psychiatry when he wrote Adolf Meyer requesting an opportunity to study under him. His work with Clérambault was a second manifestation of this interest, but it was not until many years later—when he accepted an appointment as director of the Illinois State Psychopathic Institute in 1951—that this interest was to come to the fore.

In 1928 Bailey was selected by Dallas B. Phemister, professor of surgery at The University of Chicago, to develop neurological surgery at that institution. Bailey was thrilled with this opportunity. His earlier experiences at The University, when he had associated with such outstanding neuroscientists as Charles Judson Herrick, George W. Bartelmez, and Anton J. Carlson, had demonstrated that institution's dedication to neurology.

Franklin C. McLean, who had close affiliations with the Rockefeller Institute, had been recruited by The University to organize this new medical school. McLean envisioned a new type of medical school in which clinical fields would have a close relationship, not only to basic medical sciences, but also to biological and physical sciences represented elsewhere in The University. Under such a system, both clinical and preclinical departments would engage in research. It was also McLean's plan that all members of the medical faculty be employed full time, supported entirely by salary. Phemister entertained similar views and had recruited—in addition to Bailey—Lester R. Dragstedt, head of the Department of Physiology at Northwestern University, and George Curtis, head of the Department of Anatomy at the University of Louisville, as professors of surgery.

Knowing this, Bailey was encouraged to hope that he would be able to develop an integrated department of neurosciences at Chicago and not just a division of neurological surgery. He might have had misgivings about his ability to handle the clinical side of his new position, for much of his time in Boston had been spent in the laboratory and his years in France had not trained him to perform neurosurgical operations. Ever helpful, Cushing, on learning that Bailey was going to Chicago, remarked "I don't know what is going to become of you. You will never be a neurosurgeon," (*Up From Little Egypt,* p. 126). Even Max Peet, professor of neurological surgery at the University of Michigan and later Bailey's close friend and admirer, exclaimed to this author on learning of the appointment, "Why, Bailey is not a neurosurgeon; he's a pathologist!"

If Bailey was forced to rely on his own evaluation of his surgical abilities, in the end, he was proven correct. He became a superb neurosurgeon, though he lacked the enthusiasm for operating that characterizes most surgeons. Once he had demonstrated he could perform an operation well, he lost interest in repeating it and would turn successive operations of the same type over to me.

Bailey arrived at The University of Chicago in the summer of 1928 and immediately began organizing a department of neurosciences. As his neurosurgical assistant he recruited this author, Paul C. Bucy, then a young man. Trained in neuropathology by Samuel T. Orton, I had developed an interest in the pathology of brain tumors. He also brought in Roy R. Grinker, the son of Bailey's old teacher of neurology, Julius Grinker, as medical neurologist. Stephen Polyak was induced to come to Chicago from the University of California, where he had recently completed the research that resulted in his publication *Afferent Fiber Systems of the Cerebral Cortex* (Berkeley: University of California Press, 1932, 370 pp.). Bailey intended to recruit into his new department men with backgrounds in both neurochemistry and in neurophysiology.

At first all went well at Chicago. Bailey, together with a number of colleagues in other departments of The University, formed a "neurology club." This group, very informal, with no dues, no bylaws and no officers, met monthly except during the summer. At each meeting one of the group presented the results of his own research, followed by a general discussion and free-swinging criticism. No notes were kept and there was no publication. In addition to Bailey, the neurology club included the famous physiologist Anton J. Carlson; physiologist Arno B. Luckhardt, discoverer of the anesthetic properties of ethylene and father of modern anesthesiology; Robert R. Bensley, head of the Department of Anatomy and expert on the islet cells of the pancreas; Charles Judson Herrick, world-renowned comparative neuroanatomist and neurological philosopher; George W. Bartelmez, embryologist, neuroanatomist, and experimental endocrinologist; Roy R. Grinker, neuropathologist, medical neurologist, and later psychiatrist and psychoanalyst; Carl R. Moore, endocrinologist and chairman of the Department of Zoology; Karl S. Lashley and Heinrich Klüver, two of the world's most distinguished experimental psychologists; Ralph S. Lillie, neurophysiologist; Nathaniel Kleitman, physiologist and authority on sleep; Paul Weiss, experimental neurologist later at The Rockefeller University; Ralph W. Gerard, electroneurophysiologist; Stephen Polyak, neuroanatomist and clinical neurologist; Frederick C. Koch, biochemist; Paul C. Bucy, neurosurgeon; and A. Earl Walker, in training in neurosurgery and studying the thalamocortical connections. It was a most stimulating group that established the scientific atmosphere for the development of the neurosciences, not only at The University, but in all of Chicago as well.

Yet when The University of Chicago was approached about receiving a large gift to create a neurological institute with Bailey as director, with The University to raise an equal sum of money from other sources, it informed the prospective donor that it was not interested. This seemed clear evidence that The University was not interested in becoming an outstanding center for the neurosciences.

The Division of Neurology and Neurological Surgery, of which Bailey was head, was a hydra-headed monster. Bailey himself operated under heads of three separate departments: Dallas B. Phemister, surgery; George F. Dick, medicine; and Frederick Schlutz, pediatrics. Bailey found that he could rarely get all three men to agree about anything. On one occasion they could not even agree to accept a young man Bailey had selected for training in neurology and neurosurgery. When Bailey finally approached the president of The University, Robert Maynard Hutchins, and the dean of the Division of Biological Sciences, William Taliaferro, he found neither interested in developing neuroscience at The University of Chicago. After years of trying, Bailey discontinued his efforts and resigned.

It is not to be assumed, however, that the years Bailey spent at The University of Chicago were not fruitful. During this period Bailey trained this author, who later became head of the Division of Neurological Surgery at Northwestern University Medical School. Another student, A. Earl Walker became head of the Division of Neurological Surgery at the Johns Hopkins Medical School, while William H. Sweet became professor and head of the Department of Neurological Surgery at Harvard University and the Massachusetts General Hospital. Bailey was also largely responsible for training Clovis Vincent and his associates in neurosurgical techniques. Vincent was already a distinguished neurologist and was recognized as the father of modern neurological surgery in France. Marcel David, a pupil of Vincent's and ultimately pro fessor of neurological surgery in Paris, and Pierre Puech of Paris also worked with Bailey. Among Bailey's other distinguished pupils were Chisato Araki of Kyoto and Kenji Tanaka and Kentara Shimizu of Tokyo, who were to return to Japan and foster neurosurgery there. Other pupils were Cobb Pilcher, professor of neurosurgery at Vanderbilt; Sidney Gross, head of the Department of Neurosurgery at Mt. Sinai Hospital in New York City; Adolfo Ley Gracia, professor of neurosurgery in Barcelona and the first neurosurgeon in Spain; Arist Stender, professor and head of the Department of Neurology and Neurological Surgery at the Free University in West Berlin; Jerzy Chorobski, professor and head of the Department of Neurosurgery in Warsaw; Wallace Hamby, professor of neurosurgery at the University of Buffalo and later head of neurological surgery at the Cleveland Clinic; Jess D. Hermann, head of neurosurgery at the University of Oklahoma; John E. A. O'Connell, head of neurosurgery at St. Bartholomew's Hospital, London; and Stephen Környey, professor and head of the Department of Neurology, Pecs, Hungary.

There were many others—from Italy, Belgium, Argentina, and elsewhere—who later had distinguished careers in general surgery and who benefitted from a period in Bailey's service. These included William E. Adams, professor and chairman of the Department of Surgery, The University of Chicago; Frederick E. Kredel, professor and chairman of the Department of Surgery, Medical University of South Carolina; and Henry Harkins, professor and head of the Department of Surgery, University of Washington, Seattle.

What of research by and under Bailey at Chicago? His first major publication after arriving at Chicago was a book already started while he was in Boston, *Blood Vessel Tumors of the Brain*. In 1933, he published his classic clinical text on brain tumors, *Intracranial Tumors*. His many scientific papers from this era included: "Hemangiomas of the Cerebellum and Retina (Lindau's Disease)"; "Angioblastic Meningiomas"; "Intracranial Sarcomatous Tumors of Leptomeningeal Origin"; "Oligodendrogliomas of the Brain"; "The Oxytocic Substance of the Cerebrospinal Fluid"; "Cavernous Hemangioma of the Vertebrae"; "Contribution to the Study of Tumors in the Region of the Third Ventricle"; "Astroblastomas of the Brain"; "Origin and Nature of Meningeal Tumors"; "Spongioblastomas of the Brain"; and "A Sensory Cortical Representation of the Vagus Nerve." In addition, with Buchanan and Bucy, he published *Intracranial Tumors of Infancy and Childhood*.

At this time A. Earl Walker, under Bailey's supervision and the direction of Stephen Polyak, established the connections between the various nuclei of the thalamus and the different parts of the cerebral cortex, published in the true classic, *The Primate Thalamus* (Chicago: University of Chicago Press, 1938. 321 pp.). This author, also under Bailey, had demonstrated that abnormal involuntary movements, such as choreo-athetosis and tremor, could be abolished by specific destructive lesions in the brain. As a result of my work on neural control of the skeletal musculature, I began to formulate ideas that led to my demonstration that the so-called "pyramidal syndrome" does not develop as the result of destruction of the pyramidal tract and that the pyramidal tract can be destroyed in both man and monkey without causing paralysis. Theodore J. Case, working with equipment he built himself in Bailey's laboratories, was one of the first to demonstrate the changes in the electroencephalogram as the result of a tumor of the brain.

During the years from 1928 to 1939, while he was organizing neurology and neurological surgery at The University of Chicago, Bailey was actively teaching undergraduates and establishing The University Clinics as an outstanding institution for the treatment of brain tumors and other neurological disorders.

After his resignation in 1939, Bailey accepted an appointment as professor of neurology and neurological surgery at the University of Illinois, in Chicago. Here he was relieved of all administrative duties and had his own neuropathological laboratories, both for his own use and for the use of the many graduate students who came to him. He also taught medical students and cared for such patients as interested him, continuing the practice he had started at The University of Chicago, where, during the last several years, he had entrusted most of the neurological surgery to this author's hands.

In 1937 Bailey's research interests were to take a somewhat different turn. He took a leave of absence from The University of Chicago for a year and a half, going first to Belgium for several months with his old friend from Boston days Frederic Bremer, one of the leading neurophysiologists of Europe. From there Bailey went to Yale to spend time with the noted Dutch neurophysiologist, J. G. Dusser de Barenne, for Bailey had long recognized that he could never achieve complete mastery of all phases of neurology unless he became involved in neurophysiology. At the University of Illinois he induced Eric Oldberg, head of the Department of Neurology and Neurological Surgery, to engage Warren S. McCulloch, a pupil of Dusser de Barenne's at Yale, to take charge of the experimental neurophysiological laboratories in the new Illinois Neuropsychiatric Institute. In this laboratory, Bailey, McCulloch, Hugh Garol, and Gerhardt von Bonin investigated the cortico-cortical connections in the brain and the functions of these in monkeys and apes. After a few years McCulloch left Illinois to go to the Massachusetts

Institute of Technology and was succeeded by Ralph Gerard, who became director of the neurophysiological laboratories for a short time.

Bailey had serious doubts about whether the minute parcellation of the cerebral cortex Cecile and Oskar Vogt and their pupils had described was either accurate or meaningful. Collaborating with Gerhardt von Bonin, professor of neuroanatomy at the University of Illinois, he concluded that only major cytoarchitectonic areas in the cerebral cortex could be documented. From these studies came two books, *The Neocortex of Macaca Mulatta* (1947) and *The Isocortex of Man* (1951). Bailey conducted some investigations on the physiology of the midbrain with Edward W. Davis, but probably the most significant of his studies at that time were made with Frederick A. Gibbs on temporal lobe epilepsy.

After the new Illinois Neuropsychiatric Institute was opened and Bailey's laboratory established, graduate students from all over the world came to work with him. Some of these, like John R. Green, director of the Barrow Neurological Institute in Phoenix, Arizona, took their residency training in neurological surgery at the University of Illinois. Others came to work with Bailey for only a few months, or a few years. Among these were Carl Graf, professor of neurosurgery at the University of Iowa; Carlos Oliveras de la Riva, professor of neurology, Barcelona, Spain; B. Griponissiotis, professor of neurosurgery, Thessaloniki, Greece; H. R. Oberhill, associate professor of surgery (neurosurgery), Northwestern University; Rudolf Petr, professor of neurosurgery, Hradec Králové, Czechoslovakia; Roman Arana Iniguez, director of the Neurological Institute, Montevideo, Uruguay; Joseph G. Chusid, associate clinical professor of neurology, Columbia University; F. E. Nulsen, professor and head of the Department of Neurological Surgery, Case Western Reserve University, Cleveland; John D.

French, director of the Brain Research Institute, University of California, Los Angeles; Oscar Sugar, professor and head of the Department of Neurological Surgery, University of Illinois, Chicago; José G. Albernaz, professor and head of the Department of Neurology and Neurological Surgery, University of Minas Gerais, Belo Horizonte, Brazil; Bernard Pertuisset, professor of neurological surgery, Paris; Orlando Andy, professor and head of the Department of Neurosurgery, University of Mississippi.

Bailey was also the editor for ten years (1946-1956) of the neurosurgical section of *The Year Book of Neurology, Psychiatry and Neurosurgery* . He participated in the translation of his books *Intracranial Tumors* and *Tumors of the Glioma Group* into several different languages and in the publication of new editions of *Intracranial Tumors* and *Intracranial Tumors of Infancy and Childhood*. He became very interested in the possibility of stereotactic surgery in man but realized that such operations could not be performed satisfactorily without an accurate atlas of the human brain. Bailey recognized the practically insuperable difficulty of obtaining suitable fresh specimens of human brains in the United States. He secured the cooperation of an old friend from Boston days, Georg Schaltenbrand, who was professor of neurology at the University of Würzburg, in Germany. Schaltenbrand was able to obtain one hundred and eleven brains and have them properly fixed, sectioned in various planes, stained, and photographed. The result was *Introduction to Stereotaxis with an Atlas of the Human Brain*, published in three volumes (Stuttgart: G. Thieme, 1959). This atlas was promptly accepted because of its accuracy and the excellence of the photographs of the brain.

But Bailey's interest in neurology and neurological surgery was lagging, and he returned to a former interest—psychiatry. Bailey had long been interested in the relation ship of the brain to human mentation and human behavior and was convinced that many psychiatric problems resulted from organic disturbances in the structure and functioning of the brain. He was also convinced that psychiatry had been "led down the primrose path" by Sigmund Freud and that psychoanalysis was the principal stumbling block in the way of scientific progress in psychiatry. In *Sigmund the Unserene* (1965), he wrote:

> My animus is not directed toward Freud. My animus is directed toward the overweening, hypertrophied and distorted influence which his movement has attained in these United States, as he foresaw and feared. In this way, it has, in my opinion, done great damage to psychiatry, as well as to our civilization in general. . . . (p. xiii)
>
> There is no conclusive evidence that, as a method of therapy, psychoanalysis is more effective than others, and it is costly beyond its merits; as a philosophy it is chaotic, contradictory and circular; as a science it is unestablished; and as a religion it is inadequate. (p. 103)

When, in 1951, he was offered positions as director of the Illinois Neuropsychiatric Institute, research and educational consultant to the Illinois Department of Public Welfare, and director of the Illinois State Psychopathic Institute, Bailey saw the opportunity to do something for psychiatry. In these positions he had the onerous responsibility of visiting and reporting on the care of patients in various state psychiatric hospitals in Illinois. He was also the advisor to the governor of Illinois in psychiatric matters. He very shortly realized that no worthy psychiatric research existed in Illinois, that there was no psychiatric training in state institutions, that state institutions were very understaffed, and that what staff there was were poorly trained. He also noted that care of patients in the Illinois state psychiatric institutions was woefully inadequate. He also recognized that, even if better-trained personnel were available in sufficient numbers for these state institutions, therapeutic knowledge in psychiatry was so terribly deficient that they would not be able to do much for these unfortunate patients. Adequate, effective therapy is dependent upon understanding the cause of disease and its pathology. This information was, and in large measure still is, sorely lacking.

Bailey learned that over $8 million was lying unused in the treasury of the state of Illinois, money that had been paid over the years by patients' relatives for their care. Under the laws of the state this money could only be used to improve the care of patients in the state psychiatric institutions, yet surprisingly, up until this time, no one had had the imagination necessary to use it. Bailey was able to convince Governor Adlai Stevenson and the state legislature to use these funds to create and maintain an Illinois Psychiatric Training and Research Authority, which was modeled after the National Institute of Mental Health. Its purpose was to support psychiatric training and research within the state. Bailey was named executive director of this Authority. As long as Bailey was in good health and able to protect it from politicians eager to control it, it continued to function in an exemplary fashion.

At the same time that the Authority was created, Bailey convinced the governor and the legislature of Illinois to build the Illinois State Psychiatric Institute in Chicago. This institute of 500 beds was to be organized and staffed by the five medical schools in Chicago. It housed patients and facilities for research for the training of young psychiatrists, primarily for the staffs of the other state psychiatric institutions. Bailey was named director of research at the new institute (1958-1967). In 1964 he was also appointed director, Division of Research Services, Department of Mental Health, State of Illinois, a position he held until 1967. It would be toying with the facts not to report the failure of these efforts to improve psychiatry and psychiatric patient care in the state of Illinois, a great disappointment to Bailey. He did not accomplish what he had envisioned, but he did do much to stimulate a reevaluation of psychiatric concepts and what passed for psychiatric knowledge and to reorient psychiatry in the direction of science.

Bailey also "took off" after Freud, believing that Freud's deification and the conversion of psychoanalysis into a religious creed—to be accepted on faith—was a roadblock to the proper understanding and effective treatment of psychiatric disorders. He explored Freud's writings in the original German, reading and citing 318 articles—26 by Freud himself—in the Norman Wait Harris Lectures delivered at Northwestern University in April 1963 and in his book *Sigmund the Unserene: A Tragedy in Three Acts* (Springfield, Ill.: Charles C Thomas, 1965), later translated into French under the title *Sigmund le Tourmenté* .

Bailey says in his introduction to this book (p. xi), "Today no intelligent man can avoid coming to grips with his [Freud's] powerful, more baneful than beneficial, influence." It is not to be supposed that the pernicious influence of the Freudian doctrine was limited to the understanding and practice of psychiatry. As Alajouanine, professor of neurology at the University of Paris, says in the preface to *Sigmund le Tourmenté* , "Dans les sphères intellectuelles, beaucoup croient avoir trouvé dans les conceptions freudiennes une psychologie nouvelle qui va permettre de pénétrer dans les profondeurs de l'inconscient et, de là, pour certains, va s'édifier une philosophie de la vie et une interprétation du monde basée sur la métapsychologie de Freud. Dans le domaine littéraire, le roman, le théâtre, la critique et même l'histoire sont de plus en plus largement imprégnés de concepts tirés des doctrines freudiennes."

Bailey's psychiatric friends and teachers in Paris had been impressed that Freud was little concerned with fact and quite prepared to accept as fact the fanciful, often imaginary, frequently inaccurate statements of his neurotic and psychologically disturbed patients. This was not only apparent to these men—many of whom had come to know Freud during his stay in Jean Martin Charcot's clinic (October 13, 1885, to February 28, 1886)—but was also known from Freud's own writings. Freud states in his autobiography (1952) in referring to "childhood scenes" that his patients related to him, "I believed these stories, and consequently, supposed that I had discovered the roots of the subsequent neurosis . . . when, however, I was at last obliged to recognize that these scenes of seduction had never taken place, and that they were only phantasies which my patients had made up, or which I myself had perhaps forced upon them." as quoted in *Sigmund the Unserene*, p. 19.

It is not to be supposed that Bailey's lectures or books about Freud abolished his "baneful influence" on psychiatry, literature, and thought, but it is fair to say that Bailey's efforts in the field of psychiatry were a major force in diverting psychiatric thinking back into scientific channels. Bailey was unhappy with what he had been able to do in psychiatry, just as he had been unhappy years before with the failure of his efforts to bring neuroanatomy, neurophysiology, neurochemistry, neuropathology, medical neurology, and neurological surgery together into one discipline in our universities. Bailey was ahead of his time.

Bailey was a scientist—a seeker after truth by the establishment of facts and intolerant of dishonesty. On one occasion I was in his office when he was reading a scientific article in which a distinguished neuroanatomist described intracellular inclusions he was attempting to correlate with certain functional activities. A puzzled look came over Bailey's face and he reached in his desk for a magnifying glass to examine the photomicrograph carefully. Finally, he straightened up and said, "That photomicrograph has been retouched." Bailey promptly wrote to the author, whom he knew well, asking if the photomicrograph had been retouched. Receiving a letter back saying that it had not, Bailey concluded: "He has lied," and he never referred favorably to that man again. So far as I know he never saw him, spoke to him, or corresponded with him.

Yet, on another plane, one of Bailey's favorite quotations was from Mark Twain, that one should never spoil a good story by telling the absolute truth. Bailey was a delightful raconteur, and the reader is well advised to refer to *Up From Little Egypt*. To one who heard and enjoyed these stories on many occasions, it was obvious that, from time to time, the stories varied and one could never be sure of the "absolute truth."

Yet Bailey's intense striving for scientific truth in himself and in others led at times to difficulties. He was not popular with many of his contemporaries and was feared because he was so blunt and outspoken. Early in his career he attended a meeting of the American Neurological Association with his chief, Harvey Cushing. He sat near the front of the room. Three prominent members from New York City gave papers. First Frederick Tilney presented a paper on the pituitary gland, a subject with which Bailey was very familiar. When Tilney sat down, Bailey (not yet a member) rose to his feet to say that he did not believe what had been said. Shortly thereafter, Walter Timme gave a paper on the pineal body, which in Bailey's opinion was even worse than the first. He got up a second time to say so. The third paper was by Smith Ely Jeliffe, who reported that he had "cured" a boy with a sarcoma of the thigh with psychoanalysis. Bailey promptly rose to his feet a third time, but felt a tap on his shoulder. Harvey Cushing beckoned him out of the room, and when they got to the hallway, said to him agitatedly, "What are you trying to do? Ruin your career? You will never become a member of this organization if you keep this up. Those three men are the most influential members of the American Neurological Association." Bailey subsided for the moment, but it would be an exaggeration to say that he, too, had been "cured."

Bailey loved his family—his wife Yevnigé, his daughter, Irene, and his son, Norman. During the last several years of his life, Yevnigé devoted almost every hour of her life to his care. In her own right Yevnigé was a distinguished musician, yet she subjugated her talent and interests to being Percival Bailey's companion and helpmate. This did not go unappreciated. On many occasions Bailey spoke of how fortunate he had been to have her as his wife.

Following his marriage on October 25, 1923, one of Bailey's principal interests was the Armenian people and their history. For many years he longed to go with his wife to visit Armenia, a state in the Soviet Union bordering on Turkey. One attempt was frustrated at the Yugoslav border. Finally, he received an invitation from the Armenian Academy of Science to lecture at the All Soviet Physiological Congress in Yerevan, the capital of Armenia. This was the opportunity for which Percy and Yevnigé had been waiting, and the trip proved to be all they had anticipated. Not only did Bailey lecture at the Congress, but he and his wife also took advantage of the opportunity to visit historical sites and other parts of the country.

In addition to his immediate family, Bailey had a second family—those who had trained with him. Without exception these men, whether they had spent a few weeks, months, or many years under his tutelage, greatly admired and respected him. Bailey never tried to take credit for the work of his associates, as heads of other departments not infrequently do. He was always generous with his time and would help his men with their investigations, spend hours with them over the microscope, and help them with their writing. He was always available to discuss personal problems and to advise about many matters, particularly about plans for the future. If he thought that one of his men was considering a position that offered less opportunity than the man deserved, he said so. He was careful in his letters of reference and recommendation, lavish with praise when it was deserved, but never misleading. He taught his men in two ways—by his own example and by giving them the opportunity to find out for themselves.

Perhaps more than anyone else who was associated with him, I had the opportunity to see and appreciate all of these things. We were associated closely from the late summer of 1928 until his death in 1973. I was particularly privileged in this respect. For years we shared the same office, with our desks on opposite sides of the same room. Although our ages were not very different—he was twelve years older than I—our relationship at first was more that of father and son. Later our relationship became that of two brothers. In addition to being generous with his time and his knowledge, he was also at times generous with his money. His salary at The University of Chicago was always minimal. Yet on one occasion, when he was unable to obtain the agreement of the three department heads under whom he was supposed to work regarding the selection of a new resident and the payment of his salary, Bailey took the money from his own small salary to pay the man.

Bailey, in addition to being an excellent raconteur, wrote well of subjects other than science and medicine. He was a popular dinner guest at many fraternities and was invited to many student meetings. His tales of his life in Paris were enthusiastically welcomed throughout the campus. For many years he was a member of the Chicago Literary Club, of which he was president from 1954 to 1955. The Club met every Monday night, except during the summer months. Bailey attended religiously and presented papers on many occasions. The quality of the papers and the enjoyment of the hearers could be judged by the size of the audiences. When Bailey spoke, the club rooms were crowded. Bailey's literary abilities are further evidenced in *Up From Little Egypt*, a collection of autobiographical vignettes. It is not an autobiography, nor was one ever written. Fond of quoting Mark Twain, he was often heard to remark, "As Mark Twain said, 'if no man ever yet told the truth about himself, it was because no one ever could.'"

Politically Bailey was a liberal and a Democrat. It is not surprising then that he often found fault with the American Medical Association and what it did and what it did not do. It was once pointed out to him that the policies and actions of the Association could not be changed unless men like himself were willing to participate actively in its affairs. He replied, "How could I possibly have anything to say which would influence the American Medical Association?" It was pointed out to him that it would be a simple matter to get him elected to the House of Delegates of the Association and that once there he could exert his influence. He was dubious but agreed to serve if elected. He was elected as the delegate of the Section on Nervous and Mental Diseases, a fact which he omitted from his *curriculum vitae*, though he did list his chairmanship of the Section on Nervous and Mental Diseases (1944). After one term as delegate, he had had all he wanted of medical politics and refused to be reelected. One term, however, gave him little opportunity to influence the course of the Association.

As the director of the National Institute for Neurological and Communicative Disorders and Strokes (NINCDS) informed me, Bailey was never appointed to a position of im portance in the National Institutes of Health because the FBI disapproved of his liberal ideas. No greater error of judgment could have been made. Bailey was a dyed-in-the-wool midwesterner, loyal to the United States and proud of his country. Even more important, he could have made valuable contributions to NIH and to the NINCDS.

Percival Bailey's neurological interests were broad and included neuroanatomy, neuropathology, neurophysiology, medical neurology, neurological surgery, and psychiatry. In the United States he was elected president of the leading neurological and neurosurgical societies—the American Neurological Association and the Society of Neurological Surgeons. He also held honorary membership in some twenty-five foreign medical and scientific societies. He was frequently invited to speak and delivered, among others, the Hughlings Jackson Lecture of the Montreal Neurological Institute and the Otfrid Foerster Lecture of the German Neurosurgical Society. He served as visiting professor at many universities, both in this country and abroad. He was made an Honorary Doctor of Science by two of his alma maters, Southern Illinois University and The University of Chicago. The honor of which he was most proud was *docteur honoris causa de l'Université de Paris* , bestowed on him in 1949. His other numerous degrees, honors, and society memberships are listed at the end of this memoir. Throughout the world Bailey was recognized as the man with the broadest grasp of the nervous system. In every part of the field, he was Mr. Neurology.

Bailey's international recognition as an outstanding teacher, scientist, and neurosurgeon is well illustrated by a quotation from Clovis Vincent, professor of neurological surgery in Paris. In his inaugural lecture, Vincent paid the following tribute to his friend and colleague:

> Bailey est mon ami. Grâce à lui, en quelque jours, j'ai compris la neurochirurgie américaine; grâce à luije n'en ai pas vu seulement le dessus, mais aussi le dessous. À lui, j'ai pu poser des questions auxquelles il a répondu avec conscience et amitié, comme quelqu'un qui veut vous apprendre quelque chose. On peut dire que Bailey a été le trait d'union entre la neurochirurgie américaine et moi.

During the last few years of his life, Bailey suffered from two distressing illnesses. Neither the cause nor an effective treatment was ever found for either. Without warning he would have recurring bouts of chills and fever and, on occasion, would become delirious—spells that would last for days and incapacitate him. The possibility that this might represent an obscure form of malaria was considered but never proved. Quinine, for a short time, seemed to help, but it soon became apparent that this optimism was false. From time to time he also suffered from severe and extremely painful stomatitis. This would last for days, or even for a week or two. Here again the cause remained obscure and no treatment proved effective.

Another disability that plagued Bailey greatly was the loss of all useful vision in one eye and some blurring in the other, the result of a retinal degeneration. For a man who had spent a good share of his life at a binocular microscope, this was a severe blow. It greatly impaired his ability to continue with his pathological studies, although he still had an eagle eye for details that escaped many others.

In February of 1967, a real tragedy struck. It was a cold, windy, icy day in Chicago, and Bailey went to his office at the Illinois State Psychiatric Institute by taxicab. As he was walking from the cab to the building, he slipped on the ice and fell. He had some pain in his hip but did not believe that he had been seriously hurt. He remained at work, but when he returned home late in the afternoon he was so confused that he could not tell Yevnigé what had happened. She was not aware that he had fallen or had pain in his hip, only that he was incoherent. She took him to the hospital, and for days his physicians despaired of his life.

It was not until a week after the accident that he became able to tell his wife and his physicians about the pain in his hip. X-ray examination then revealed that he had impacted the head of his femur into the pelvis, but his general condition was too poor to permit any attempt to reduce this fracture-dislocation. The joint ultimately became ankylosed, and when he was better, the disability with his hip greatly limited his ability to get about. For the rest of his life, this hip was his greatest burden.

Slowly he improved. At first he was able to move only with the help of his wife, who spent every moment, awake or asleep, with him. Later he mastered the use of two crutches and finally was able to get out of his house for short periods. Fortunately he remained alert and intensely interested in everything. For several years he welcomed my neurosurgical residents from Northwestern University to his home for an evening. On these occasions he would entertain them for hours about his own experiences, with vignettes from neurosurgical history, or with tales about such outstanding figures as Harvey Cushing or Pierre Marie. It was also during this period of enforced inactivity that he compiled autobiographical sketches into a book, *Up From Little Egypt*.

One chapter is missing from that book. "Pepper Pot" is about Harvey Cushing and Bailey's associations with him and was delivered before the Chicago Literary Club.[2] With his usual candor and consideration, Bailey sent a copy of "Pepper Pot" to Cushing's daughters, asking their approval for its publication. To his surprise he got back a letter threatening

[2] A text can be found in the Club's archives at The Newberry Library, Chicago.

him with a lawsuit if it were ever published. Advised by several distinguished legal friends that such a suit could never succeed, Bailey yet elected not to publish "Pepper Pot." As he said, "They have much more money than I do."

During the six years from 1967 until his death in 1973 (ages seventy-five to eighty-one), his greatest burden was his enforced inactivity and his dependence on his loving wife. There were marked fluctuations in his condition during this period, but the general level of his mental and physical health remained about the same. But in June of 1973 he became persistently less alert, at times confused, at others lethargic. The overall trend was now definitely downhill until August 10, 1973, when he became confused, then semicomatose, and died within a couple of hours.

The world had lost one of its most outstanding men—a man of catholic interests, both general and scientific—a truly renaissance man, the likes of which we shall probably never see again. And I lost a close personal friend and second father.

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Eric G Ball

Eric Glendinning Ball

July 12, 1904-September 4, 1979

By John M. Buchanan and A. Baird Hastings

During his seventy-five years, Eric Glendinning Ball witnessed and participated in the maturation of biochemistry as a major biological science in the United States. As a graduate student in chemistry he applied his analytical skills to the estimation of the chloride content of blood and serum. As a postdoctoral fellow and young instructor, he turned his attention to oxidation-reduction potentials of various naturally occurring organic systems. When enzymes were recognized as proteins susceptible to isolation and purification as individual entities, he measured the potentials of several biological oxidation-reduction systems, notably those of the cytochromes and xanthine oxidase. Eric considered his research in this area his most important contribution to science. Yet his work during the war years on the cultivation of the malaria parasite in vitro, and his postwar ventures into the study of the role of hormones in the synthesis of lipids by fat pads of the rat were equally significant, reflecting his application of biochemistry to problems in cell physiology. Like many another biochemist, Eric transformed himself from chemist to biologist as the application of chemical methods to emerging areas of biology became possible.

Eric was born on July 12, 1904, in Coventry, England, the first of two children of Nellie Glendinning and Charles

Sturges Ball. A sister, Margaret, completed the Ball family seven years later. Eric emigrated to this country with his parents at the age of ten months. His father, Charles, had entered the ministry in the Wesleyan Methodist Church in England and remained affiliated with the Methodist Church following his arrival in the United States. During the next eight or nine years, however, Charles Ball studied at various divinity schools in this country. His religious viewpoint changed during this time, and he became a Congregationalist. Later, at the age of fifty, he joined the Episcopal Church and began a new career of teaching and preaching.

Charles Ball served in turn on the faculties of Goucher College and the divinity schools at Gambier, Ohio, and Alexandria, Virginia. Thus, as is frequently the case in ministerial families, Eric experienced a constant change of habitation and environment. After successive moves from New Rochelle, New York, to Bridgeport, Connecticut, followed by short stays in New Haven and Kensington, Connecticut, the Ball family returned to England for a year. It was here, at age seven, that Eric first experienced some measure of independence from family supervision and began to follow his bent for exploring the English countryside and drawing, in precise detail, various natural objects such as leaves and flowers. He was to continue to enjoy outdoor life and the thrill of following a new trail for the remainder of his life. Undoubtedly, with maturity, these new trails became scientific ones.

Upon returning to the United States, the Ball family lived for a while in Stony Creek, Connecticut, and then moved to Lansford, Pennsylvania, in the heart of the anthracite coal-mining district. Finally, in the fall of 1917, the family moved to Baltimore where Eric entered Baltimore City College. Apparently he was a lackluster student in high school, possibly because of a lack of inspiration or motivation. Undoubtedly his life must have been greatly influenced by the prolonged illness of his mother, who died in 1919.

It was a course in chemistry, taken as a requirement for graduation from high school, that directed his interest to the sciences and led to his enrollment in Haverford College as a chemistry major. Although achievement in his studies was at first difficult because of insufficient background, Eric gradually gained strength academically and demonstrated his true scholastic caliber during his senior year, when he compiled the highest grades of his college career. At the same time, he earned letters in soccer and track and was manager of the basketball team. This reversal of form won for him, on graduation in 1925, the Scholarship Improvement Prize and a Clementine Cope fellowship to carry on graduate work at Haverford the following year. His thesis work for the master's degree at Haverford was concerned with the melting points of mixtures of sodium sulfate and sodium chromate. Although the results of these experiments never reached publication, the year's work gave Eric the experience he needed to launch a career of research in science.

Although he had planned to continue graduate work for his doctorate, possibly in physical chemistry, following award of his master's degree, Eric took a job in a paper factory to replenish his financial resources. At this point, an opportunity arose that altered his entire career. D. Wright Wilson, head of the Department of Physiological Chemistry at the University of Pennsylvania, offered Eric a position as a research assistant. Eric attributed this stroke of good luck to a friendship between the Wilson family and his father, who had performed the marriage ceremony for Wright and Helene Connett some years earlier. At closer inspection, however, it appears that other, more personal circumstances may have been responsible for this joining of Eric's fortunes to those of the Wilson family. Helene's younger sister, Edith Connett, had introduced her friend Grace Snavely to Eric while he was a master's candidate at Haverford. A courtship ensued that resulted in their marriage on September 10, 1927.

By this time, Eric had registered as a graduate student in the Department of Physiological Chemistry and was well on his way to completing his doctoral dissertation under Wright Wilson. The results of his work, "A Study of the Estimation of Chloride in Blood and Serum," were published in 1928 in the *Journal of Biological Chemistry*. A subsequent piece of research was published in abstract form during the following year in the *American Journal of Physiology*, and later in the *Journal of Biological Chemistry* (1930). It described the composition of pancreatic juice and blood serum as influenced by the injection of inorganic salts. Although the character of his research was to change markedly in subsequent years, Eric did return to his first interest in physiological chemistry with publications in 1936 and 1941. The latter research, which used "C-bicarbonate, was one of the first projects undertaken after his arrival at Harvard Medical School as a newly appointed assistant professor of biochemistry.

Although his Ph.D. was formally awarded in 1930, Eric had been granted a National Research Council fellowship in 1929 to work with W. Mansfield Clark in the Department of Physiological Chemistry at The Johns Hopkins University. An earlier interest in physical chemistry had been stimulated by James C. Andrews at Pennsylvania. Andrews was himself a physical chemist, and he had organized a seminar for a handful of graduate students on the application of oxidation-reduction potentials to biological systems. Through this seminar, Eric became acquainted with Clark's work on the determination of the hydrogen ion concentration and his first ten papers on oxidation-reduction studies.

After a year in Baltimore, Eric planned to spend a year with Otto Warburg at the Institut für Zell Physiologie in

Berlin-Dahlem, Germany. Dr. Warburg was undoubtedly the world's leading expert on the enzymes of biological oxidation-reduction systems, and further training in this exceptional laboratory would have prepared Eric for his ultimate goal of applying his training as a physical chemist to these enzyme systems. Nevertheless, this projected year in Germany was postponed for seven years because of an offer from Hopkins of an instructorship—an exceptional opportunity, particularly at that time when the country was slipping into one of its most prolonged depressions. Thus, from 1930 to 1937, Eric investigated the oxidation-reduction potentials of a number of biologically important materials including adrenaline, ascorbic acid, echinochrome, phthiocol (the pigment of the human tubercle bacillus), lapacol, lomatiol, and various other hydroxynaphthoquinones.

Early in his academic career, Eric established a lasting connection with the Marine Biological Station at Woods Hole, Massachusetts. As his bibliography reveals, many of his research projects, presumably accomplished during the summer months, were concerned with marine biological products. During the summer of 1931, he became interested in the report that isotonic solutions of sodium chloride from certain sources caused hemolysis of fish red blood cells. Since isotonic saline was used extensively in biological research, particularly with marine organisms, it was imperative that the identity of this hemolytic factor be established. The results of an example of his remarkable "scientific sleuthing" were presented at the April meeting of the American Society of Biological Chemistry in 1932. One of us (A.B.H.) was fortunate enough to be present in the audience and gained a firsthand impression of a systematic and logical analysis of the problem and of the speaker himself. (Improbably, the factor turned out to be silver ions, which were inadvertently supplied from silver-coated vessels used in the processing of so dium chloride in some instances. At this trace concentration of silver ions, the solubility product of silver chloride is not exceeded.)

These summers at Woods Hole ultimately led to Eric's election as a trustee of the Marine Biological Laboratory in 1942 and, for a term (1953-1958), of the Woods Hole Oceanographic Institute. The Balls also established a beautiful summer home in Woods Hole overlooking Nantucket Sound.

During his tenure at Johns Hopkins only one of his several papers appeared in collaboration with Clark. This was due in part to Clark's paternal relationship to his younger faculty and his wish that they receive full recognition for their accomplishments. One amusing incident in this regard deserves recording. In one of Eric's studies, a rather complicated apparatus was required. As an expert glassblower, Clark had spent considerable time in its construction, and Eric felt that his name should appear as a collaborator. As was the custom at that time, papers were usually channeled through the department head for submission for publication. Without Eric's knowledge, Clark removed his own name and instead appended the phrase, "with the technical assistance of W. Mansfield Clark." This may well be the only instance on record when a department head served as the technical assistant of a junior instructor.

At last, in 1937, with a grant from the Guggenheim Memorial Foundation, the Balls spent an exciting, stimulating year in Berlin-Dahlem in Warburg's laboratory. The contrast between the scientific atmosphere and approach to research prevalent in the United States and that in Germany at the time was very evident, particularly in Warburg's laboratory. Europe was then the center of the rapidly developing disciplines of biochemistry and enzymology. Aside from Warburg, Eric had also met and admired Hugo Theorell, who two years previously had spent a sabbatical year in Berlin-Dahlem where he had purified cytochrome C and demonstrated that flavin is the cofactor of D-amino acid oxidase. Other current European luminaries were Richard Kuhn, Hans von Euler, Richard Willstatter, and Otto Meyerhof.

The central research focus at that time was the understanding of the enzymatic processes of physiological oxidation-reduction systems, as well as those of fermentation and glycolysis. Considering the depth of scientific and intellectual richness in the Europe of that time, Eric must have felt a certain degree of pride in his own contribution to research in this area. During his sabbatical leave, he was able to isolate and purify xanthine oxidase and demonstrate that it contained flavin as a cofactor. In addition, within a remarkably short time, he measured the oxidation-reduction potentials of three known components of the cytochrome system. This piece of work was an important contribution to our understanding of the pattern of electron flow within the biological oxidation system. In recognition of these achievements, Eric received the 1940 Eli Lilly Award in Biochemistry from the American Chemical Society. In 1948, he was awarded an honorary doctoral degree from his alma matter, Haverford College. In conferring the degree, Haverford's president cited Eric as "a conscientious and valued teacher of biological chemistry, a productive scientist whose research has pioneered new frontiers of chemistry and medicine."

In retrospect, it seems particularly appropriate that Eric should have been recognized for both his contribution to research *and* teaching. On his return to Hopkins in 1938 as war clouds gathered over Europe, Eric received an invitation from one of us (A.B.H.) to join the faculty of the Department of Biological Chemistry at Harvard Medical School as an assistant professor, with the stipulation of promotion to associate professor within a year. Arriving at Harvard in the fall of 1940, Eric had barely enough time to establish his labo ratory and continue his work on the cytochrome system when the United States entered the war in December 1941.

With the involvement of the department head (A.B.H.) in the Committee on Medical Research in Washington, Eric became acting head of the department in 1943, a position he held for three years. Simultaneously, he undertook responsibility for two new studies: first for a research project on mustard gases and later for a study involving the cultivation of the malaria parasite in vitro. During this latter period, Eric also served as secretary of the Panel on Biochemistry of Antimalarials, and in this capacity he joined the horde of wartime commuters to Washington, D.C. For this work he was awarded a certificate of merit by the U.S. government and the Ordem du Cruzero do Sul by the government of Brazil.

At the conclusion of the war, there was an extensive expansion of medical research and teaching facilities. Eric was approached to head the Department of Biochemistry at Western Reserve Medical School with the charge of developing a new medical curriculum that integrated the preclinical medical sciences. He refused the offer, but since this new approach to medical education was attractive to him, President Conant of Harvard University proposed that Eric develop a comparable program for graduate students as chairman of the Division of Medical Sciences. Conant also proffered the further possibility that such a newly developed curriculum would be extended to medical students in their preclinical years. With this new responsibility, Eric was promoted to the rank of full professor in 1946. Sixteen years later, in 1962, he became the Edward S. Wood Professor of Biological Chemistry.

Between 1946 and 1952, a great effort was made to design a new approach to teaching the premedical sciences, to raise money for the program, and to attract a number of excellent graduate students to Harvard Medical School. The fall of

1952, when Eric assumed the chairmanship of the Division of Medical Sciences, saw the attainment of many of his goals. The total enrollment of graduate students in the division had risen from about five to nearly fifty. Some $17,000 was available annually for fellowships, and a new integrated course was inaugurated with the aid of a grant from the Commonwealth Fund for $200,000 for a three-year period. Among other things, this program fulfilled an urgent need for many returning veterans who were establishing their roots in the academic community. Undoubtedly, Eric considered his role in this program as one of his major contributions, not only to Harvard but also to the national educational effort in the medical sciences.

The flow of excellent graduate students into the Division of Medical Sciences was reflected in the significant number of those who elected to carry out their graduate research with Eric, who was himself undergoing a change in his research interests. By the 1950s, many of the basic biochemical reactions of cellular metabolism had been discovered, and there was a growing inclination to study the regulation of metabolism in both prokaryotic and eukaryotic cell systems. In view of his longstanding interest in oxidative-reductive reactions, it was not surprising that Eric would choose to study lipid synthesis in the interscapular brown adipose tissue of the rat and in epididymal fat pads. This biosynthetic reaction requires the utilization of both reduced triphosphopyridine nucleotide and adenosine triphosphate (ATP). In vivo, the synthesis is under hormonal control.

> Of particular importance was the discovery by his group of the antilipolytic action of insulin in 1962 and his quantitative determination of the flow of carbon atoms through the major pathways of carbohydrate and fat metabolism in 1964. His discovery in 1966 that lipogenesis from glucose was limited in its maximum rate, not by the catalytic activity of any of the enzymes involved in the process, but by the amount of ATP produced as

a by product of the process, introduced an entirely new element into our concepts of metabolic control. His interests in adipose tissue metabolism were very broad, extending from a study of the role of brown adipose tissue in the production of heat accompanying arousal in hibernating rodents to hormonal mechanisms which allow migratory birds to draw upon their caloric reserves during flight.

After his retirement in 1971, Eric continued a research program on marine biological products at his laboratory at the Marine Biological Laboratory in Woods Hole. Winter months were spent by the Balls in their apartment in Ozona, Florida.

In addition to those honors and professional activities already mentioned, Eric was elected to the National Academy of Sciences in 1948 and to the American Academy of Arts and Sciences in 1945. He was a long-term consultant to the Eli Lilly Company and served in a number of editorial capacities on the *Journal of Biological Chemistry*, *Biochemistry*, and *Biochemical Preparations*. He was a member of several professional societies including the American Society of Biological Chemists, American Chemical Society, Biochemical Society of Great Britain, Society of General Physiologists, and the Endocrine Society. He was also a fellow of the American Association for the Advancement of Science. In 1963 he was awarded a Guggenheim Fellowship for the second time for a sabbatical leave at the Scripps Clinic and Research Foundation in La Jolla, California. As a Commonwealth Fund Fellow, he was a visiting professor at the Oswaldo Cruz Institute, Rio de Janeiro, in 1964.

Altogether, he published approximately 150 articles in various scientific journals. In 1973 he published the book *Energy Metabolism*, which contained the essence of the unique lectures entitled "Biological Oxidation and Its Control" that he had delivered over the years to medical students. Eric was a superb lecturer, succinct and concise, with his material organized in precise detail. He was well respected and liked, both by medical and graduate students. It was his sad duty at certain times to counsel medical students who were, temporarily at least, in some academic difficulty. These students were known as members of the Ball team.

Eric was known for his many endearing personal qualities and for his enjoyment in entertaining at home, whether for dinner or a game of bridge. It was inevitable that as a summer resident of Woods Hole he should become devoted to the marine sports of boating and fishing. Many graduate students and younger colleagues will recollect their fishing excursions from Woods Hole in Eric's appropriately named skiff, the *Red Devil*. Those trips were devoted to simple bottom fishing and so permitted the participants to engage fully in long scientific and general discussions. On such occasions, the full warmth of Eric's personality was manifest, as well as his wisdom, his perceptive approach to innumerable matters, and his abiding faith in young scientists.

In all parts of his personal and scientific life, Eric was generously supported by his loving wife, Grace. (To her friends, however, she has always been known as "Gracie" in recognition of her elfin, blithe personality.) At the time of his death on September 5, 1979, they had been married happily for nearly fifty-two years.

In the conclusion of the memorial minute published in the *Harvard Gazette*, it was stated that "His colleagues and his former graduate students mourned his passing, but celebrated his many contributions to science and to graduate education in biochemistry." These few terse words are an epitaph that would have pleased Eric, and certainly most succinctly express our appreciation and affection for him as a man, as a scientist, and as an educator.

In preparing this biography, the authors are indebted to notes left by Eric and to a memorial minute written by seven of his former students and colleagues: J. M. Buchanan, J. T. Edsall, A. B. Hastings, M. L. Karnovsky, B. L. Vallee, T. H. Wilson, and C. A. Villee. The minute appeared on June 27, 1980, in the *Harvard Gazette* (vol. 85, no. 39, p. 6). Direct quotations from this article have been made at times in this memoir because restatement could have improved neither the meaning nor the sentiment.

HONORS AND DISTINCTIONS

Chronology

1919 U.S. Citizenship
1925 S.B., Haverford College
1926 A.M., Haverford College
1930 Ph.D., University of Pennsylvania
1942 A.M. (hon.), Harvard University
1949 D.Sc. (hon.), Haverford College
1926-1928 Assistant, School of Medicine, University of Pennsylvania
1929-1930 National Research Fellow, Johns Hopkins Medical School
1930-1933 Instructor in Physiological Chemistry, Johns Hopkins Medical School
1932 International Physiological Congress Fellow, Rome
1933-1940 Associate in Physiological Chemistry, Johns Hopkins Medical School
1937-1938 Guggenheim Memorial Foundation Fellow, Institut für Zell Physiologie, Berlin-Dahlem
1940-1941 Assistant Professor of Biological Chemistry, Harvard Medical School
1940 Eli Lilly Award in Biochemistry
1941-1946 Associate Professor of Biological Chemistry, Harvard Medical School
1941-1945 Official Investigator on two OSRD contracts
1942-1970 Trustee, Marine Biological Laboratory, Woods Hole
1943-1946, Acting Head, Department of Biological Chemistry,
1958-1959 Harvard Medical School
1944-1946 Secretary, Biochemical Panel, Board for Coordination of Malarial Studies, Washington
1945 Visiting Professor, University of Brazil Medical School
1945 Ordem du Cruzero do Sul (Order of the Southern Cross, Brazil)
1946-1962 Professor of Biological Chemistry, Harvard Medical School
1946-1958 Consultant, Eli Lilly Company
1948-1956 Editorial Board, *Biochemical Preparations*; Editor-in-Chief, Vol. 2 (1952)
1948 Certificate of Merit
1950-1960 Editorial Board, *Journal of Biological Chemistry*

1952-1968 Chairman, Division of Medical Sciences, Harvard Medical School

1953-1957 Trustee, Woods Hole Oceanographic Institute

1959 Commonwealth Fund Fellowship, Great Britain

1962-1970 Board of Associate Editors, *Biochemistry*

1962-1971 Edward S. Wood Professor of Biological Chemistry, Harvard Medical School

1963 Guggenheim Memorial Foundation Fellow and Visiting Investigator, Scripps Clinic and Research Foundation, La Jolla California

1964 Commonwealth Fund Fellow, Brazil. Visiting Professor, Oswaldo Cruz Institute Rio de Janeiro

1964 Fuller Albright Lecture, Peripatetic Club

Memberships

National Academy of Sciences
American Academy of Arts and Sciences
American Society of Biological Chemists
American Chemical Society
Biochemical Society of Great Britain
Fellow of the American Association for the Advancement of Science
Society of General Physiologists
Endocrine Society
Sigma Xi
Alpha Omega Alpha (hon.)

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Carnegie Institution, Stanford, California

Jens Christian Clausen

March 11, 1891-November 22, 1969

By C. Stacy French

Observers of nature—from primitive man to the most enlightened modern scientists—have long speculated on the relative importance of heredity versus environment in the development of living beings. With regard to humans the subject is so explosive that many fear to learn more. With regard to plants, however, the issue of development raises no controversy; experiments can be carried out in peace and results interpreted rationally. Working as the head of a plant biology research group at the Carnegie Institution, Jens Christian Clausen successfully clarified—for certain species and under certain conditions—the question of heredity versus environment so basic to biology.

When still a student in Denmark, Jens Clausen became interested in the genetics of a wide variety of local violet found near his home. A farm boy with sharp powers of observation, he had a mind that always asked why. His interest in living things eventually took him to Copenhagen University for his B.Sc. and M.Sc. degrees and, in 1926, the Ph.D. in the new field of genetics, and then to an assistant professorship at the Royal Agricultural College under Øjvind Winge—a scholarly botanist whom the young farmer-student held in considerable awe.

In the 1920s, while Clausen was making his name with his studies of Danish vegetation, Harvey Monroe Hall, professor of botany at the University of California, Berkeley, and a research associate of the Carnegie Institution, began transplanting native plants into contrasting environments. Supported by the institution, Hall and two student botanists, William M. Hiesey and David D. Keck, concentrated scattered transplants into three gardens with very different environments: one near sea level at Stanford University, one at an elevation of 4,500 feet at Mather on the western edge of Yosemite National Park, and one at 10,000 feet at Timberline in the High Sierra of Yosemite's far eastern edge. In 1932, Hall invited Clausen to join his group as a geneticist. But a few months after Clausen's arrival, Hall died, leaving Clausen to take over as the project's director.

Jens Clausen's vigor and enthusiasm enabled him to spend long hours in the field and made him a natural leader and delightful colleague. A devoted Christian, Jens's faith reinforced a naturally strong character and joy in life, never limiting his independence of thought. He introduced many a famous botanist to the California vegetation of the mountain stations, and many had the good fortune, after a strenuous day of fieldwork, to enjoy his warm hospitality at the Mather "Hog Ranch" cabin.

In 1959, at the request of one of his students, Jens wrote a brief autobiography, which—written in his own words—fortunately preserves for us something of his spirit:

CONFESSIONS AND OPINIONS OF AN ECOLOGIST OF SORTS

Personal Background

Unfortunately, I must confess to being born in 1891—in the latter part of the nineteenth century. After a younger brother died when he was five and I ten years of age, I became, essentially, an only child.

I cannot claim much formal schooling because I went through only two grades of a four-grade, every-other-day country grammar school in Denmark, attending the two upper grades of this school between the ages of eight and thirteen. The principal of the school, who was also the teacher of the two upper classes, had advised my father to spare me from attending the beginner's classes by not starting me in school until I was past eight. He remained a personal friend of mine as long as he lived, but I must confess that I put little effort into the class work. Instead I did considerable extracurricular reading.

The grade school was followed by one year in a private, local secondary school, where I was introduced to the fundamentals of English, German, world history, physical and natural sciences, and mathematics. At the age of fourteen I left school entirely and took up the farming of my parents' fifteen-acre place. My father had been a house-builder during my early boyhood, and as I took over the daily running of the family farm, he resumed his primary interest. Unlike him, I had no inclination toward the building trade but was highly interested in farming. As a consequence, I never attended formal high school (or gymnasium as it was called in Denmark), but at the age of twenty-two presented myself for the entrance examination to Copenhagen University—an affair lasting a full month—and was admitted. Half a year later I had my B.Sc. degree at the University.

As far as my early education, I was largely autodidactic. I learned to read at the age of four using the daily newspaper as a primer and asking my father the meaning of the words. Curiosity was a driving force, and my father, who himself had been a quick learner, was a sensible person. My mother had never gone to school but learned at home. Before I normally would have started to school, I had learned reading, writing, and basic arithmetic. These skills opened the world of books to me, and being brought up on a farm I also be came familiar with all kinds of living things and with farm practices. At various times during the early years one learned the principles of physics and chemistry from everyday experiments and had fun constructing primitive microscopes and telescopes.

My first introduction to botany was given me at the age of nine by an uncle who owned my mother's 5-acre birthplace in a botanically interesting part of the country, sculptured by high moraines and watercourses. My uncle was a farm laborer on a neighboring larger farm, but he was highly intelligent, interested in botany, and had by himself learned to recognize most of the Danish wild plants. I spent short summer vacations there, and on weekends he took me along on hikes over hill and dale and through forests. These trips opened a new world to me.

During my early teens, I borrowed from the county library Eugenius Warming's recently published book, *Plantesamfund*, the Danish forerunner of his later, *Ecology of Plants*, and considerably more inspired than its English successor. I became deeply interested in this subject, and during my high school years I made a detailed study of the botanical communities within a 2,000-acre moor area near my home and wrote a kind of term paper on the subject as part of my botanical training.

I likewise studied geology during my teens on small private expeditions around the country and on a trip to the famous Kinnekulle region in central Sweden, which contained a complete succession of the Cambrian and Silurian deposits. I returned from such expeditions with considerable paleontological and botanical loot. My home was also near primitive sites of middle stone age kitchen middens, and near remnants of a neolithic lake-dweller's community where stone axes of great artistic beauty had been manufactured for trade some 4,000 years ago. The hills were studded with burial sites from bronze and early iron age, uniting the past with the present.

News of the rediscovery of Mendelism drifted through the local newspapers, and in high school I also bought the sixth edition (1906) of Darwin's, *The Origin of Species*, in English. Receiving some private tutoring from Mr. Thorgiles, an unusual teacher who had become headmaster of the secondary school I once attended, I was now able to expand on my previous introduction to the sciences, mathematics, and the history of the civilizations of the world. Mr. Thorgiles, more than anyone else, was responsible for introducing me to the scientific method. A new grasp of foreign languages also opened German and English literature to me.

Therefore, although I did not attend formal high school, I probably had better training, going on my own, with a little guidance here and there. Life during those later teens was interesting and absorbing, as I managed a small dairy farm, pursued liberal studies of many kinds, and was church organist and church school teacher on the side.

My original plan had been to go to the Royal Agricultural College in Copenhagen as a preparation for a farming profession. From 1910, however, at the age of about nineteen, I was also a part-time teacher at the secondary school I had attended a few years earlier, teaching primarily science. This experience was absorbing, and I decided to change plans and attend the university instead. Starting at Copenhagen University in 1913 at the age of twenty-two, I majored in botany and minored in physics, chemistry, geology, geography, and zoology. In 1920, at the age of thirty, I received my master's degree in natural history and geography. During my student days, I continued to teach in the school but gradually tapered off on farming. I commuted the 30 miles to Copenhagen certain days of the week for the mandatory laboratory courses and some lectures. Two years—1916 to 1918—were spent in military service during World War I. At that time, stationed only 8 miles from Copenhagen, I commuted by bicycle.

The University of Copenhagen was a true university rather than a school. It did not have residence requirements and one more or less developed one's own plans for study in consultation with the professors. There were excellent opportunities for discussions with professors and with other students. Chresten Raunkiaer was my major professor in botany, P. Boysen Jensen in plant physiology, and Wilhelm Johannsen in plant physiology and genetics. I knew Eugenius Warming, who at that time was retired but still highly interested in the young students. August Krogh was my professor of animal physiology. I started physics under Niels Bohr, followed by H. M. Hansen, chemistry under Einar Biilmann and Chr. Winther, and geography under H. P. Steensby.

Intellectually, it was a highly stimulating environment. We were a small group of graduate students in biology who met for discussions, developing foundations for new approaches to systematics and ecology, sparked by the young science of genetics. In 1917 Winge defended his doctoral thesis on the significance of the numbers of chromosomes in plants, in which he proposed the polyploidy theory.

When I had my first interview with Wilhelm Johannsen in 1913, I mentioned that, for my master's degree, I wanted to choose a specialty in genetics, and that I was interested in combining the genetic with the ecological approach to the study of systematics. Johannsen had no use for ecology and was rather amused at the suggestion. Genetics was still new at the time, and although Johannsen was one of its pioneers, nobody had ever before specialized in genetics. It was finally arranged that I should have a specialty both in systematics and genetics. At Raunkiaer's suggestion I chose the *Violaceae* because they were supposed to contain many natural hybrids.

Just at the time when Winge developed the polyploidy theories, I found that *Viola tricolor* had thirteen and *V. arvensis* (a close relative) seventeen pairs of chromosomes—not a polyploid situation. Moreover the two species hybridized at their points of contact in the wild, and the hybrids were moderately fertile. It so happened that spontaneous hybrid colonies of these two species of violet were located a short distance from the headquarters of the artillery company to which I was assigned, and I set up my microscope on the office desk of the company command. This was undoubtedly one of the queerest cannons in artillery history!

After the war I toured Denmark studying the wild populations of these two *Viola* species. I found prostrate, perennial races of *Viola tricolor* on exposed maritime sand dunes and annual, erect races inland—although often in close proximity to the maritime ones. Seedlings of the two kinds retained their identities even when grown remote from the coast. *Viola arvensis* was found to be associated with calcareous soils, *tricolor* with sandy soils. On neutral to faintly acid soils in the contact zones could be found swarms of interspecific hybrids, having intermediate, irregular chromosome numbers. Such spontaneous hybrids of various generations segregated similarly to the artificial hybrids. I presented these findings in two papers published in 1921 and 1922 in *Botanisk Tidsskrift*. They constitute one of the early approaches to experimental taxonomy, to studies on natural populations, and to the subject of gene introgression. These studies showed that the characters of the two species recombined at their points of contact, and that genes apparently could migrate some distance from the point of contact.

Remarkably enough, Göte Turesson's first papers on ecotypes appeared in 1922, and we discovered that, unknown to each other, we had been working on the same subject of races of species adjusted to ecologically distinct environments at sister universities only 30 miles apart, though in different countries. From that time on, there was fairly close liaison between Copenhagen and Lund across the sound.

At the Royal Agricultural College, Copenhagen, 1921-1931

After my master's degree, I started preparing for my teacher's credentials, although I had already taught for ten years. Three months later, however, in April 1921, the first genetics department in Denmark was established at the Royal Agricultural College. Øjvind Winge became professor, and I was offered the assistantship (corresponding to the rank of assistant professor). As a result I did not complete my teacher's credentials but landed unexpectedly at the college I originally had aimed for.

The field of the new department was to be basic research in genetics and not plant breeding—a far-sighted arrangement in an agricultural college. During the following ten years, the genic compositions of many kinds of plants and of the tropical freshwater fish, *Lebistes reticulatus*, were analyzed; the existence of sex chromosomes in several dioecious plant species was discovered; it was found that experimentally induced cancers of sugar beets and mice had abnormal chromosome numbers. We also studied interspecific hybrid progenies of several groups of plants of the genera *Melandrium*, *Geum*, *Tragopogon*, *Erophila*, and *Hypericum*. The papers relating these results are in Winge's name and much has never been published, but it was an excellent experience to work with so many different kinds of organisms.

On my own time, during evenings and vacations, I continued the investigations of the violet species of the Melanium section. These experiments resulted in a series of papers that were published in *Hereditas* between 1923 and 1931, and two papers on chromosome numbers and relationships of species published in *Annals of Botany* between 1927 and 1929. Mrs.

Clausen, although herself not a trained biologist, was a dedicated and skillful helper in the delicate and time-consuming work of crossing, pollinating, and classifying the large F_2 progenies, and of fixing and embedding the buds for cytological investigations.

My doctoral thesis, "Genetical and Cytological Investigations on *Viola tricolor* L. and *V. arvensis* Murr.," was published in *Hereditas* in 1926. As far as I know, this is the first demonstration of the fact that taxonomic characters distinguishing species are controlled by genes that can be analyzed. In Denmark, as in other Scandinavian countries, the doctorate is based on advanced research, the investigations are conducted after one has ceased being a student at the university, and there are no faculty advisors. The doctorate carries with it the right to lecture at the university on subjects of one's own choosing and to conduct courses there.

In 1927, I was granted a Rockefeller fellowship for one year at the University of California at Berkeley. In 1929, together with E. B. Babcock, who became a lifelong, close friend, I published a paper on chromosome pairing in three interspecific hybrids of *Crepis*. But the highly varied and diversified California vegetation, which I saw in the company of Babcock and others, had an even greater impact on my ecological thinking. In 1931, after my return to Copenhagen, I published a paper on chromosome pairing in C. H. Ostenfield's interspecific *Polemonium* hybrids.

With the Carnegie Institution of Washington at Stanford, 1931

H. M. Hall pioneered the transplant investigations in the Sierra Nevada beginning about 1921, and in 1923 cooperated with Babcock on a combined genetic-taxonomic investigation on the hayfield tarweeds, the Euhemizonia section of the genus *Hemizonia* of the Madiinae. Hall wrote me already in 1922 after my first two papers had been published that he was interested in conducting similar studies in California on plant relationships. We followed each other's work during the years and met both in California in 1927, and in Denmark in 1928. In 1930 I was unexpectedly offered a position as cytologist (later biologist) in his new program on experimental taxonomy, after the department of plant biology of the Carnegie Institution was established at Stanford in addition to the earlier stations in the Sierra Nevada. I accepted this offer in 1931 and arrived at Stanford in late October.

Tragically, Hall died four months later in Washington, D.C.—a great loss. I found myself unexpectedly chosen to take his place. It was fortunate for the future program that David D. Keck and William M. Hiesey, who had assisted Hall and knew the background of the plants were able to remain as part of the staff. Now began an interesting time of cooperation between men of quite different backgrounds and leanings, representing cytogenetics, ecology, taxonomy, and physiology.

Ecotype and Varied Environment Studies

Hall's transplant investigations, using plants of many genera and families that were cloned and grown in highly contrasting environments had been started to check on claims by Gaston Bonnier and F. E. Clements that lowland plants changed into alpines upon being transplanted, and vice versa. In analyzing the results of experiments under careful and constant control (published in 1940), it became obvious that no such change takes place, although the transplanted ramets are modified in their new environment.

It was more significant, however, that species widely distributed in western North America contain a fairly large number of physiologically distinct ecotypes, more so than Turesson observed in his extensive investigations in northern Europe. The most intensive sampling of natural populations came from a transect along the 38th latitude in central California, where two coast ranges parallel the coast and block the oceanic influence from the valleys. Beyond the Central Valley of California, the Sierra Nevada range paralleling the coast rises to 14,000 feet, removing the last of the oceanic influences so that the intermountain region is a desert plateau. This arrangement contrasts with the topographic situation in Europe, where the high mountains are at right angles to the coast and where the Atlantic influence is felt hundreds of miles from the coast. There are, therefore, fewer ecological zones in Europe than in California, and this is reflected in the ecotypic differentiation. A detailed analysis of natural populations and ecotypes in the *Achilles millefolium* complex was presented in a Carnegie Institution publication in 1948.

Evolution of Genetic Barriers

California species of the Madiinae of the Compositae were used in an investigation on populations and on ecotypic, interspecific, and intergenic differentiation. The species of the Madiinae are primarily diploid and have diploid chromosome numbers. More than 300 hybridization experiments have been conducted in this group of approximately eighty-five species of ten genera. The hybrids combined evolutionary entities that range over a scale from distinct ecotypes, over closely related species, to distinct taxonomic sections and genera.

As the data were assembled, it became obvious that they reflected a graded series of evolutionary separations. Morphologically distinct varieties of the same ecotype have simple genetic differences. Distinct ecotypes or subspecies of the same species are distinguished by complex gene systems, but their genes are still completely interchangeable. Farther along the scale, moderate genetic incompatibilities were encountered that resulted in weakness of the second generation and partial sterility in the first generation. In more effectively separated entities the genomes had become so differentiated that chromosomal pairing was almost eliminated in their hybrids. Even farther along, the entities were so different that they were unable to intercross, or if they crossed, the first-generation hybrid was sublethal. The details of most of these experiments are still unpublished.

Stages in the Evolution of Species

As the massed data of our own crossings were compared among themselves and with other data previously recorded in the literature, it became obvious that the evolutionary barriers to the interchange of heredities evolve gradually. There was a strong coincidence of strong barriers among species that good taxonomists had placed in distinct sections of a genus, while weaker barriers existed among closely related species of one section, the so-called ecospecies. Ecospecies tend to occupy ecologically distinct habitats, whereas remotely related species of distinct sections can occur together in the same habitat. The major lines of this development were sketched in the 1951 publication *Stages in the Evolution of Species*.

We found that evolutionary differentiation proceeds gradually from the stage of the local population to distinct ecotypes that occupy ecologically distinct zones, and to distinct ecospecies after partial barriers have evolved that prevent free gene exchange between certain of the ecotypes of the species complex. The differentiation proceeds to distinct cenospecies (species complexes whose genomes have become so different that chromosomal pairing is prevented in their hybrids but amphiploidy is still possible) and to distinct genera that are unable to intercross. Evolution is therefore reticulate until the level of the genus. From there on it becomes furcate, as Darwin represented it. The branches of the evo lutionary tree are composed of genera, not of species, for the species form an evolutionary network within the branches. (See the 1945 Carnegie Institution publication for a report of this work.)

Apomixis

A very extensive series of experiments on the evolutionary aspects of apomixis, centering around the *Poa* genus, are in their concluding stages. Even to a greater extent than amphiploidy, apomixis can lead to rejuvenation of the genus, because it enables interspecific hybrids to escape some of the grueling interspecific gene interchanges. At the evolutionary stage of apomictic reproduction, the inheritance is no longer transferred as individual genes but as huge complexes of chromosomal complements, so that, quite often, entire genomes are being added, subtracted, or exchanged. Ecologically, the apomictic interspecific hybrids are especially important because genomes with their built-in ecologic adjustments can be transferred almost whole.

Apomictic seed clones also make it possible to undertake clonal transplant experiments on a worldwide scale because the clones can be established from seed rather than from ramets of live plants. Drs. Nobs and Hiesey cooperated with me on the *Poa* project, but it will require a couple of years to complete the detailed analysis of the responses of hybrid clones in many environments, to be followed by a written report.[1]

[1] The work was completed by Hiesey and Nobs and published in 1982 by the Carnegie Institution of Washington, Washington, D.C., under the title: *Experimental Studies on the Nature of Species. VI. Interspecific Hybrid Derivatives Between Facultatively Apomictic Species of Blue Grasses and Their Responses to Contrasting Environments*.

Genetic Structure of Ecological Races

The most important step in evolutionary differentiation is the rise of distinct ecotypes. Although it is possible that some agro-ecotypes may arise within a few centuries, most of our naturally occurring ecotypes have been in position in slowly changing environments, probably for millions of years. Such has been the case with coastal and alpine ecotypes of *Potentilla glandulosa*, belonging to the worldwide diploid species complex of the section Drymocallis. The species of this section are slowly developing, long-lived plants, and although they are semiwoody perennials, they can be cloned.

Individuals of lowland and alpine ecotypes of *Potentilla glandulosa* were intercrossed twenty-five years ago for the purpose of studying the kind of genic mechanism that distinguishes contrasting ecotypes of such a diploid and probably relatively primitive species of the genus. A second-generation progeny was cloned and was studied over many years in the contrasting environments of the lowland and mountain stations of the Carnegie Institution in central California. The responses of the ramets were recorded over successive periods of years.

This experiment, based on the combination of the genetic with the transplant method, revealed many new facts on the hereditary structure of related ecotypes and on the nature of the gene systems that distinguish such ecotypes. It opened the door to several highly neglected fields, such as the genetic structure of the elementary evolutionary entities, the range of phenotype expression of the same genotype in contrasting environments, and the interrelation among genes, processes, morphological expression, and environment. (The data are presented in a 1958 Carnegie Institution publication.)

Balance Between Variation and Coherence

There has been considerable speculation as to how neighboring ecotypes can remain relatively distinct. In the F_2 segregations of hybrids between ecotypes, it has now been shown that linkage exists between a sufficient number of the genes that control the parental characters so that the parental combinations are favored. Continued natural selection at the same time tends to favor the established ecotypes. Each of the characteristics of the ecotypes are regulated by several genes located in different chromosomes, and only some of the genes that regulate two characters are linked. Such a system causes moderate genetic coherence among characteristics of existing ecotypes as long as the environments remain relatively unchanged.

On the other hand, the ecotypes of a species store a great deal of unused or inactive variability that can become released after crossing; accordingly, the F_2s of interecotypic hybrids show considerable transgressive segregation. Normally, the selection will favor the parental combinations, but in times of geologic change a great deal of the genetic variation that is stored within the existing ecotypes can become released, and new gene combinations evolve fairly quickly from recombinations among hitherto unexpressed genes of existing ecotypes.

Many of the stored genes have been repressed by inhibitors; others are inactive because their complementary genes are found in another ecotype. The mechanism of linkage, which favors the retention of present combinations as long as conditions remain the same, will also accelerate the stabilization of new combinations after crossovers have occurred and a new kind of selective pressure has started.

Each characteristic is regulated by multiple genes, some of which have opposite effects, but only one or two of the genes that regulate a couple of characteristics are involved in the linkage mechanism, whereas the remaining genes can be linked with genes controlling other characteristics. This kind of genetic structure, in which potential variability is in balance with coherence mechanisms, provides a remarkable resiliency in ecotypes and in closely related ecospecies.

Evolution of Communities

The organisms of a community must, in their later stages, have evolved together, because they have achieved adjustment not only to the same kind of environment but also to each other. The organisms that exist in the same community are usually evolutionally remotely related. In contrast, phylogenetically closely related organisms (such as ecotypes and ecospecies of the same species complex) occur in ecologically distinct although often contiguous habitats. Moderate gene migration is possible between contiguous ecotypes and ecospecies, but genetic coherence and natural selection tend to keep them distinct.

The Search for the Differentiating Processes

Recently, the work of the experimental taxonomy group of the Carnegie Institution has entered a new phase by adding physiological laboratory research to the transplant and genetic method. This approach is now followed by Drs. Hiesey, Milner, and Nobs.

An unusually well-adapted organism has been found, the *Mimulus cardinalis-lewisii* complex. Along the central California transect, this complex has ecotypes ranging from an outer Coast Range lowland race to an alpine race at 10,500 feet altitude in the Sierra Nevada. *M. cardinalis* ranges from sea level to about 5,000 feet and is adjusted to pollination by hummingbirds, whereas *M. lewisii* goes from 5,000 to 10,500 feet altitude and is adjusted to pollination by bumblebees.

Morphologically, the two *Mimulus* species are so different that some taxonomists have placed them in distinct sections. Both are diploid, having eight pairs of chromosomes. They are easily hybridized by artificial pollination, the hybrids are fully fertile, and the second and later generations are vigorous. The parents and hybrids are self-compatible, but it is necessary to pollinate them artificially because the floral structures in the hybrid are such that none of the natural pollinators succeed. The two species are perennial but can be grown to maturity in one year. They can be cloned to an infinite degree because pieces of the stems can be rooted and develop to highly uniform new plants. The two forms have excellent morphological markers, and each has several ecological races.

Drs. Hiesey and Milner have developed an instrumentarium for the measurement of the photosynthesis-respiration ratios of cloned ramets over a wide range of accurately controlled laboratory conditions. The responses of the same parental and hybrid clones at the transplant stations will also be known and can be related to the laboratory findings. Controlled growth cabinets are also being developed so that the ramets can be accurately preconditioned before they are subjected to the metabolic tests. The methodology of these approaches is still being developed, but eventually these investigations will add another dimension to the experimental taxonomy investigations.[2]

The Future of Ecology

You asked for my opinion about the future of ecology. In the preceding sketch of the latest venture at our laboratory,

[2] The report of this work was published by William M. Hiesey, Malcolm A. Nobs, and Olle Björkman in 1971 as Carnegie Institution of Washington Publication no. 628 entitled: *Experimental Studies on the Nature of Species. V. Biosystematics, Genetics, and Physiological Ecology of the Erythrante Section of* Mimulus.

you have a part of the answer. This, however, is probably not what you had in mind.

Ecology as a separate discipline and wrapped up in its own mushrooming vocabulary, I feel, is on its way out, but so is any branch of science that is sufficient to itself and refuses cross-fertilization by other sciences. I am for biology of the inclusive kind that runs from cytogenetics over physics and chemistry, to the physiological and morphological expressions of the genotype in relation to the environment, culminating in a study of the evolutionary adjustment to environment. In my own lifetime I must be satisfied with a sense of the causal coherence among these processes. If, however, your definition of ecology implies such a chain of interacting processes, then it has a great future, and it will probably take a few centuries before we will be able in detail to trace some of the simpler chains of interaction.

Depending upon your own preference, you can name this branch of science evolution of living things, experimental taxonomy, biosystematics, genecology, etc., but it is the life sciences of the future. This kind of biology goes far beyond the narrow kind that the medically inclined fraction of our scientific fraternity carves out for itself and for which it has appropriated the fair name of biology.

I hope that these confessions, effusions, and opinions of mine have not been too lengthy or have sickened you on a sensible ecology. As you may have sensed from my background, I have a great love for an all-inclusive kind of ecology, and I consider it an honor when people introduce me as an ecologist, or, for that matter, as a geneticist, a botanist, or an evolutionist, because to me these are all-inclusive terms.

I am acutely aware that, irrespective of how one may extend the analysis of the forces and processes that regulate living things, we have obviously just barely touched the surface of this marvelously intricate and nevertheless highly co ordinated mechanism we call a living plant. I suppose I was born with an innate curiosity concerning the world I am a part of myself. In the great drama of an evolving and changing world, the individual person and one's own lifetime seem of small significance, but the realization of this fact is more in the nature of a challenge than a discouragement. Learning to understand our world is a never-ending occupation.

Jens Clausen

February 27, 1959

The above account in his own words takes us only to 1959, yet Jens's career continued with vigor and originality for ten more years, filled with discoveries and well-deserved honors. The institution's policy at that time of long-term support at a frugal level allowed the experimental taxonomy group (Clausen, Keck, Hiesey, and Nobs) to achieve a unique record in botanical research for continued progress on fundamental questions of plant relationships and evolution.

A man of great enthusiasm in proposing plans for elaborate experiments, Jens was also a stimulating leader and innovative interpreter of experimental results. In addition, his team benefitted from the careful deliberation and organizational ability of Hiesey, Keck, and Nobs in crystallizing significant conclusions.

During the war years Clausen became interested in the possibility of using apomixis in the evaluation of range grass strains to select those of superior quality. About two-fifths of the United States is used for cattle grazing; thus, any information that might lead to increased growth of range grass seemed likely to be of practical value. His thought was that crossing apomictic strains of grasses originating from contrasting environments that were unlikely to have crossed in the past might produce variations with new, and possibly fa vorable, mixtures of their characteristics. The pursuit of the *Poa* work for many years led to an increased understanding of plant evolution. No super range grass strains were developed as Clausen had hoped, however, in spite of a very large-scale effort and cooperation with many collaborators in Europe and the United States.

Some of the major contributions of Clausen's group were a thorough basic study of various kinds of ecotypes and their genetic structures, analysis of the composition and evolution of native species occurring across contrasting climates in a transect across central California, and an exploration of the possibilities and the limitations of crossing facultatively apomictic species of grasses and their responses when grown in different climates.

The clear establishment of "climatic races," which are adapted by heredity to growth in specific environments, finally demolished the Lamarkian idea that the modifications in growth form induced by changes in environment could influence a plant's genetic constitution. Thus, the controversy between E. F. Clements and H. M. Hall, which had been the principal reason for the transplant studies, was resolved. Furthermore, the linkage of inherited characteristics in specific groups was made evident by diagrams illustrating the way these groups of characters were distributed in the progeny of selected crosses. It became evident that the evolution of climatic races within an interfertile population takes place by exchanges of groups of linked groups of genes rather than by the slow accumulation of single gene mutations. These experiments required years of observations over many generations of plants with large numbers of samples. Such work cannot be done under a system of annual grants with questionable stability, nor can it be pursued effectively by investigators anxious for frequent promotions.

Evolutionary cytogenetics was a young science when Clausen took it up, but his work became a classic example of its possibilities. The results of his investigations and his noncompetitive joy in doing the work and in collaborating with colleagues and students have had a lasting effect on both the subject matter and on the investigators of plant life.

HONORS AND DISTINCTIONS

1949 Mary Soper Pope Medal of Botany, Cranbrook Institute of Science
1956 Certificate of Merit, Botanical Society of America
1956 President, Society for the Study of Evolution
1959 Member, National Academy of Sciences
1959 Royal Danish Academy of Science and Letters
1959 Fellow, California Academy of Science; American Association for the Advancement of Science
1961 Named Knight of Danneborg by King Frederick IX of Denmark
1961 Honorary Fellow, Botanical Society of Edinburgh
1961 American Academy of Arts and Sciences
1961 Royal Swedish Academy of Science

CHRONOLOGY

1891 Born March 11 in Eskilstrup, Denmark, 30 miles from Copenhagen, to Christen Agustinus Clausen and Christine Christensen

1905-1915 Farmer

1913 Entered Copenhagen University

1910-1916 Teacher in Danish secondary schools

1916-1918 Artillery Corps, Danish Army

1918-1920 Teacher in Danish secondary schools

1921 Married Anna Hansen (died Palo Alto, California, August 24, 1956)

1921-1931 Research Assistant, Department of Genetics, Royal Agricultural and Veterinary College, Copenhagen

1926 Ph.D., Copenhagen University

1927-1928 Research Fellow, International Education Board at the University of California, Berkeley

1931-1956 Staff, Department of Plant Biology, Carnegie Institution of Washington, Stanford, California

1936 Lecturer, University of Copenhagen

1943 Naturalized U.S. citizen

1950 Messenger Lectures, Cornell University

1950-1961 Trustee, Berkeley Baptist Divinity School

1951 Professor by Courtesy, Stanford University

1953 Lecturer in Brazilian universities

1956 Retired from Carnegie Institution of Washington (Jens preferred the word "pensioned" and kept on working all his life.)

1962 Lecturer, Vanderbilt University

1963 Lecturer, University of Chicago and Washington State University

1963-1964 Visiting Professor of Genetics, University of California, Davis

1966 Attended 11th Pacific Science Congress in Tokyo

1969 Died in Palo Alto, California, November 22

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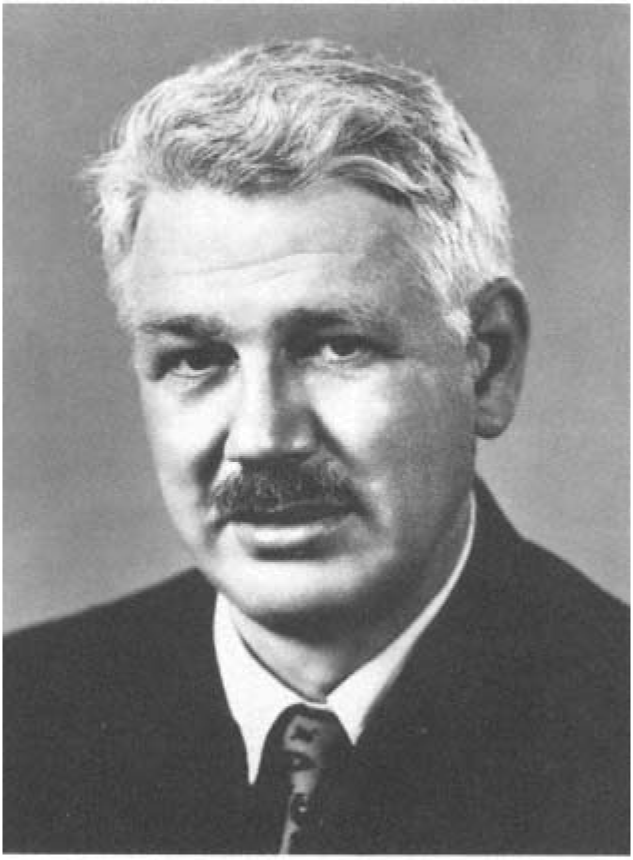

Carleton Stevens Coon

June 23, 1904-June 3, 1981

By W. W. Howells

Carl Coon was born June 23, 1904, in Wakefield, Massachusetts, a typical mélange of Yankee stock, though the Coons were originally Cornish.

At least two of Carl's forebears were Civil War veterans. His grandfather Coon—blind by Carl's time—was a great teller of tales, all calculated to make Carl very American indeed. The old man talked not only about the war, but also about his travels in the Middle East and his readings on Africa. With his cotton broker father, the young Carl made a number of trips abroad, especially to Egypt. His mother was solicitous of his education, and the family maid (also Yankee) taught him to read before he went to school.

When he was young, Carl's only apparent awareness of ethnicity came through fracases with Irish boys of the neighborhood. Pugnacious as well as scholarly, he managed throughout his early school years to avoid both distinction and opprobrium. But not entirely. His days at Wakefield High were numbered when, made fractious by boredom, he descended into the school's basement and swung from overhead pipes until they broke and flooded the place. As a cure he was sent to Phillips Andover Academy.

Actually, Carl Coon had strong intellectual tastes. His love of Egyptology began early, and he learned to read hiero glyphic writing before going to Andover. Once there, he became enamored of Greek, in which he took the prize at graduation. He learned Arabic at Harvard; but mathematics was not in him—either then or later.

At Harvard his affection for Egyptology continued, and his knowledge of hieroglyphs got him into a graduate course under G. A. Reisner. Under the great Charles Townsend Copeland, he took English composition—a subject in which he was an apt student and eventually a master. But his first exposure to E. A. Hooton caused him to veer off into anthropology.

Despite a somewhat laconic delivery, Hooton was a compelling lecturer. I myself know of at last three instances when an undergraduate, fired up by some idea in Hooton's discourse, decided to become an anthropologist then and there—Hooton the while all unwitting of the conversion going on in front of him. Coon was one of those three. Hearing about the Berbers of the Rif in North Africa with their occasional blond hair and light eyes, he determined on the spot that his first goal would be to study the lands he had long dreamed of. (Hooton himself never got nearer to Africa than the Canary Islands.)

Graduating *magna cum laude* a half year ahead of his classmates in 1925, Coon went straight into graduate school. In 1924 he had visited Morocco to sneak a look at the Riffians, who, led by Abd el-Krim, were in revolt against Spain. It was dangerous ground and therefore all the more appetizing to Carl. Reconnoitering once again in 1925, he took his plucky new bride to the just-pacified Rif to begin research for his dissertation. Hooton, keeping the Harvard community in touch with his hyperadventurous student, wrote an article for the Alumni Bulletin entitled "An Untamed Anthropologist among the Wilder Whites."

Earning his doctorate from Harvard in 1928, he stayed on in the anthropology department as an instructor. At the sudden death of Roland B. Dixon, the great ethnographer, Carl took over all his courses on the cultures of the regions of the world. Africa he knew personally. His course on Oceania, which he did not know, was one of his most absorbing. To inform himself on the peoples of Asia and Siberia, he traveled in the USSR. He was to teach anthropology at Harvard for twenty years, with time out for service in the Army in World War II.

Anthropology in the 1920s, both physical and historical, was still a relatively young science. It was intrinsically colorful, even romantic, and not nearly so methodical and specialized as it would become. This freedom of approach suited Coon's temperament, giving his originality wide scope and allowing him to explore peoples with gusto. With his natural flair and engaging writing style, he soon became well known to the public.

That he was colorful, and that he made his material so, does not mean to say that he was unsystematic. Rather, untrammeled by a plethora of guidelines, his modes of organization set the example for others. With great mental energy and insatiable curiosity, he was a prodigious reader and notetaker. He was left handed, and I always saw him at meetings writing on a pad of foolscap, his left arm curled over the page. More important, he was an outstanding firsthand observer—the prime qualification for anyone in his kind of work.

It is difficult to see how he managed to file and organize the great body of information he dealt with—but, despite his flamboyant image and undoubtedly mercurial temperament, he was a careful organizer. An enormous intellectual vigor allowed him to follow up hypotheses without becoming wedded to them. Never a writer of small papers, he looked for the larger significance. It may be said that Coon's major con tributions to science were the fruitful formulations that followed from his assimilation and organization of massive amounts of information.

PHYSICAL ANTHROPOLOGY: RACIAL ADAPTATIONS

Carleton Coon's *The Races of Europe* (1939) began as a revision of W. Z. Ripley's 1900 work but ended as a new opus that used every scrap of published information on living populations and prehistoric human remains-and much recorded history besides. Though some of Coon's hypotheses seem dubious today, they allowed him to structure a mass of material in a way that remains impressive. This book was reprinted some years later and is still regarded as a valuable source of data.

In 1933 he published a novel, *The Riffian*, a product of his predoctoral studies in North Africa. In the late 1930s he collaborated with Harvard's E. P. Chapple on *Principles of Anthropology* (1942), an ambitious quantification of the interactions of speech and action among human individuals and groups.

Coon's desire was to use Darwinian adaptation to explain the physical characteristics of race. He defined these as the physical features that distinguish modern populations and in 1950 published, with S. M. Garn and J. B. Birdsell, *Races: A Study of the Problems of Race Formation in Man*. He was exasperated by what he called the "hide-race" attitude of people who, from social or philosophical motives, seemed to deny the existence of obvious biological differences. He became indignant at any suggestion that his interest in race derived from racist motives. Although a good many articles had been written about environmental adaptation for such traits, this book was the first to address the problem as a whole.

In 1962 he brought out his magnum opus, *The Origin of Races* (1962), based primarily on human fossil material

—a synthesis that remains unmatched today, even by Franz Weidenrich. Yet his much criticized hypothesis that five subspecies of *Homo erectus* evolved separately and in parallel into *Homo sapiens* adversely affected appreciation of the book. Coon later wrote that the stark wording of this theory had resulted from a misunderstanding with his editor, and in later editions the passage was rewritten. Yet it is the first version that is still widely quoted in discussions of hypotheses of human evolution. Coon developed objective criteria for distinguishing his two species, or grades, of *Homo*. He applied these systematically and successfully, and they have not been materially improved upon. His original interpretation incorporated the evidence of virtually all fossil material then known, which the book presents with exemplary completeness. The work remains both readable to the layman and useful to the specialist nearly thirty years later. In 1965, he published a companion and sequel to *The Origin of Races* with E. E. Hunt, Jr., *The Living Races of Man*.

Coon's last book, published posthumously in 1982, *Racial Adaptations* , was a culmination of his efforts to marshall the evidence—now including biochemical data—and to suggest explanations for physical variation in man.

CULTURAL ANTHROPOLOGY

Coon learned Greek early, he profited from good teachers (including Hooton) and had a natural ear for English, which he wrote wonderfully well. His correspondence blossomed with fresh metaphors, but the hallmark of his style was its simplicity. He turned out book after book, ranging from the technical to the popular, from site reports, to texts, to travellogues, to novels. In addition to *The Riffian* (1934), he produced *Flesh of the Wild Ox*, a fictional account of his life in the Rif. *Measuring Ethiopia* is his exuberant account of his 1935 adventures gathering ethnographic data in that country one step ahead of Mussolini's troops.

More important was his 1945 *The Story of Man*, a high-level popular book on human evolution and development. His vast store of knowledge and his writing ability combined to make this book both lucid and authoritative.

Yet his knowledge was not confined to physical anthropology alone. In 1948 he became curator of ethnology at the University of Pennsylvania Museum in Philadelphia, a post that he held until the early 1960s. His 1948 *A Reader in General Anthropology*, an anthology of firsthand descriptions of various peoples, proved as successful as his *Story of Man*. In 1951, his *Caravan: The Story of the Middle East* introduced the layman to the peoples of Islam. He described present-day hunting and gathering societies in *The Hunting Peoples* (1971).

In the early days of television, he appeared on "What in the World," an educational program dealing with various objects in the collections of the University of Pennsylvania Museum. Froelich Rainey, the museum's director, would present objects to a panel of anthropologists who undertook to identify them without previous knowledge of their provenance. Carl was apt to recognize them on sight, but as a born showman and teacher, he held back. Instead of blurting out, "Of course, a Fiji cannibal fork!" he would take note of the wood, speak of stylistic resemblances, and talk of other clues that might give away the object's area of origin before giving the answer.

EXCAVATIONS AND FIELDWORK

The opposite of a museum-bound scientist, Carl's first love was the field. With competence in archaeology and ethnology as well as physical anthropology, he excavated (while on sabbatical leave in 1939) a cave in Tangier, where he found deposits going back to Mousterian times. Recovering part of a maxillary bone with Neanderthal-like morphology, he returned after the war with a Harvard team led by Hugh Hencken to complete the excavation. In 1948 he began exploring caves in Afghanistan and northern Iran, working with the University of Pennsylvania Museum. This led to another book, *The Seven Caves*, in 1952. He later investigated a cave in Sierra Leone, finding Lower Paleolithic implements but no fossils. On one occasion, when being shown around excavations at Jebel Irhoud in Morocco that had produced an important premodern skull, he spotted a second skull of the same type—a find never credited to him in print by the excavation director.

Still more than studying ancient man, however, Carl loved to observe remote and seldom-visited living peoples. His predoctoral expedition among the Riffians was only the first of many. In 1929 he went to northern Albania to observe the Gheghs, undoubtedly the most isolated people in Europe, who became the subjects of *The Mountains of Giants* , in 1950. In 1959, he joined a team of physiologists travelling to Tierra del Fuego to study the few remaining Alakaluf Indians' bodily adaptation to a cold, wet environment, which they endure with very little clothing. His posthumously published, autobiographical *Adventures and Discoveries* gives firsthand accounts of these and many other expeditions.

WORLD WAR II

During World War II, Carl Coon's knowledge of remote peoples involved him in a number of adventures well-suited both to his abilities and his tastes. As he recorded in *A North Africa Story: The Anthropologist as OSS Agent* (1980), he was recruited in deepest secrecy before the 1942 Allied landing in North Africa to stimulate an uprising against Spain among the Rif tribes, if Spain should decide to join the Axis powers. A plan to send him to Albania was later scrapped when the

Allies landed in Italy and southern France. While still a civilian, Carl performed many special undercover errands, often posing in uniforms of his own devising as a British officer. He also invented an explosive designed to to look like mule dung that would blow the treads off German tanks. He was later commissioned with the rank of major, and was invalided home after being hit on the head by a roof tile dislodged in a bombing attack.

TEACHER, COLLEAGUE, FRIEND

Throughout his life, Carl Coon remained a great teacher. He welcomed anthropologists of every level, from senior to the most junior, to his home in West Gloucester, Massachusetts, on the edge of the Ipswich marshes. He discussed with them whatever he was working on. He gave out his ideas on recent discoveries and publications, praising and disputing with equal warmth. He did not trouble himself with the relative significance of his own discoveries, concentrating rather on solidly demonstrating specific findings. Although pleased with his major books, he may have failed to appreciate their effect (not, however, lost on his colleagues) as models of construction and formulation. Despite the constant theme in his work of human variation as the result of adaptation to environment and his voluminous memory for information, he was ever one to complete a task and move on.

Reflective though he certainly was, Carl's temperament was not calm. His thought and speech both carried an edge of urgency. An entertaining if sometimes extravagant conversationalist, he brought to speech the same gift for phrasing that he so amply displayed in writing. Listener as well as raconteur, he was modest despite his flamboyance and totally devoid of self-importance. He was also honest and candid with his opinions whether they were popular or not. He was a constant, generous, and enormously rewarding friend, and—remembered over fifty years—his kaleidoscopic style brings me vivid mental pictures and inward smiles.

Carleton Coon was often honored. He won the Legion of Merit in 1945 for his war service, and was made a *membre d'honneur* of the *Association de la libération française du 8 novembre, 1942*. He won the Viking Fund Medal and Award in Physical Anthropology (1952) and the Gold Medal of the Philadelphia Athenæum (1962) for *The Origin of Races*. He was a fellow of the American Academy of Arts and Sciences and was elected to the National Academy of Sciences in 1955. He was president of the American Association of Physical Anthropologists for 1962 and 1963. He was a member of Sigma Xi and was elected to Phi Beta Kappa in 1950 at the time of his twenty-fifth class reunion, repairing a small omission indubitably caused by his eagerness twenty-five years earlier to get busy with the Riffians.

In 1926, Carl married Mary Goodale. Their children are Carleton Stevens Coon, Jr., and Charles Adams Coon. Carleton, Jr., entered the U.S. Foreign Service and, when his father died, had just been appointed ambassador to Nepal at the same time that his wife became ambassador to Bangladesh. Charles Coon is a real estate broker in Gloucester and a bridge player of international stature.

Carleton Coon, divorced, married Lisa Dougherty Geddes in 1945, the cartographer who drew the maps for many of his books. She became the companion of all his postwar work and travel. From first to last he travelled beyond the calls of his field work, to see and inform himself about areas and people. Despite deteriorating eyesight, he never stopped writing—which he called his only hobby. After holding several serious ailments at bay for some years, Carl died on June 3, 1981, at his West Gloucester home, shortly before his seventy-seventh birthday. His brilliance left a lasting mark on a generation of anthropologists.

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René Jules Dubos

February 20, 1901-February 20, 1982

By James G. Hirsch and Carol L. Moberg

René Jules Dubos, microbiologist and humanist-philosopher, was professor emeritus at The Rockefeller University at the time of his death in New York City on his 81st birthday, February 20, 1982. His name calls to mind a tall, vigorous, rosy-cheeked man, with durable white wisps on a balding head, intense blue eyes behind thick glass lenses, a shy yet broad smile, and beautiful large hands that enthusiastically punctuated every sentence. He was a spellbinding speaker and a prolific author. His charming French accent and his perfect command of English made any contact with him memorable. Whether it was a private conversation or a public lecture, he always spoke with the knowledge of a scientist, the eloquence of a poet, and the wisdom of a philosopher.

René was born in Saint-Brice-sous-Forêt, France, on February 20, 1901, and grew up in Hénonville, another small Île-de-France farming village north of Paris. His parents, Georges André Dubos and Adéline De Bloëdt, ran a butcher shop in each of these villages. René attended a one-room school where discipline was strict and students taught one another. He was a husky boy, fascinated by sports, especially bicycle racing and tennis, but at age eight he suffered a severe attack of rheumatic fever that incapacitated him for more than a year and left him with damaged heart valves. Early in his youth he was also found to be severely near-sighted, a condition that required thick corrective lenses. These afflictions instilled in him a fear of possible blindness and of a shortened lifespan, a fear that he never showed but that nonetheless caused him to live with special intensity and purpose. In place of typical childhood activities, René developed traits that would dominate the rest of his life. He walked and explored the countryside, a pastime that helped him cultivate a meditative mood—what he called the beginning of his freelance spirit. He also read avidly in history and literature, finding his earliest heroes in French translations of stories about Buffalo Bill and Nick Carter.

The family moved to Paris when René was thirteen years old. Within months, his father was called to World War I. Shortly after his return in 1918, he fell ill and in 1919, died. The raising of three children (René, his brother Francis, and sister Madeleine) and the management of the family shop were left to his mother. René helped run the butcher shop while continuing his schooling at the Collège Chaptal. At fourteen, he read Hippolyte Taine's essay on La Fontaine and was introduced to the concept of the environment as a molding force on historical events, particularly on the human psyche.

At age eighteen he applied to the École de Physique et Chimie, but another attack of rheumatic fever caused him to miss the entrance examination. After recovering he took the next test that came up, in economics, and was pleasantly surprised that he did well, ranking fourth out of 400. He was admitted to the Institut National Agronomique and excelled in all courses except microbiology—an intensely boring course, he later recalled, that dealt solely with taxonomy. He neither enjoyed nor excelled in chemistry and told his mother that this was certainly the last time he would walk into a laboratory. In his third year he won a scholarship sponsored by the government of Indochina for studies of agriculture and technology in the École d'Agriculture Coloniale in Paris with a required period of service in Southeast Asia, but was later disqualified because of his rheumatic heart disease.

In 1922, René obtained a position in Rome on the staff of the International Institute of Agriculture, a branch of the League of Nations. For two years, as associate editor of the *International Review of the Science and Practice of Agriculture* for the Bureau of Agricultural Intelligence and Plant Diseases, he abstracted journal and agricultural reports from all over the world. He now spoke Italian and English as well as French and German. René recalled his days in Rome as very pleasant. He was a handsome young man with a bushy head of hair who was particularly attracted to English girls, ostensibly to improve his language skills. At this time he was undecided about career goals, considering occupations as divergent as journalist and scientist.

In the course of his translation duties René encountered an article that he considered the major influence in his life. While sitting in the Palatine Gardens on a warm May day, instead of reading about fertilizers in a semipopular journal, he turned to an article by the famous Russian soil microbiologist Serge Winogradsky, then at the Pasteur Institute in Paris. In it Winogradsky stated that microorganisms should be studied not in a pure laboratory culture but in their own environment in competition with other bacteria. He emphasized interactions of organisms under natural conditions and the significance of the role played by the environment in these interactions. René said his scholarly life began with these ideas—ideas he restated in many forms throughout his life. (Although the two men never met, Winogradsky pre sented René's paper, based on his Rutgers thesis research, at the Académie des Sciences in Paris in 1927.)

This experience played a major role in his decision to become a bacteriologist. But René did not know how to begin until he met the American delegate to the International Institute of Agriculture, Asher Hobson, a professor of economics from the University of Wisconsin. Hobson urged Dubos to emigrate to America and even offered to lend him money. René took a course in bacteriology at the University of Rome, earning extra money to pay for his passage to America by translating books on forestry and agriculture into French. In 1924, at a conference on soil science in Rome, Hobson introduced Dubos to Dr. Selman Waksman, who was then a distinguished bacteriologist at Rutgers University. René's duties as technical assistant during the Congress included showing Dr. and Mrs. Waksman around Rome. Fate intervened a few weeks later when René set sail for America and found that the Waksmans were fellow passengers on the steamship, *Rochambeau*. They had plenty of time to talk during the crossing; Waksman was delighted to hear of Dubos's ambitions and, learning René had no definite plans, offered him a small fellowship as one of his graduate students at Rutgers.

René arrived in America and went to New Brunswick with the Waksmans that same evening. Three years later he completed his doctor of philosophy degree, doing thesis research on the decomposition of cellulose by soil bacteria. He credited Waksman with helping him develop an ecological concept of microbiology through an understanding of the relation between biochemical and biological processes. Dubos earned extra money working part time as an animal caretaker at nearby Johnson & Johnson, tutoring the research director's children, washing laboratory glassware on holidays, and translating papers on poultry pathology for a young professor.

It was just about this time that René, a budding scientist with an abstract humanist education, read Lewis Mumford's *Sticks and Stones* . René said this American author influenced his social philosophy by making him realize that institutions exist not to foster political or economic power, but to serve human needs and thereby broaden the quality of human life. Moreover, Mumford wrote about subjects related to sciences and humanities in earthy terms that described sensory experiences of daily life. Mumford's writing had a lifelong effect on this impressionable young European trying to understand American ways and to express himself in English.

René had no special plans after graduation, except for wanting to move from the field of soil science to deal with more fundamental biochemical problems. His application for a National Research Council Fellowship was rejected because he was not a citizen. The secretary who sent the rejection letter penned a note at the bottom recommending that he consult with a fellow Frenchman, Alexis Carrel, at The Rockefeller Institute in New York. This chance event led René to The Rockefeller, where he was destined to spend some fifty years of his life. Carrel was kind and considerate but had no special advice. He took him to lunch and there, whether by chance or prearrangement, René was seated next to Oswald Avery. Dubos and Avery liked each other immediately, spending not only the lunch hour but most of the afternoon discussing René's experiences with soil enrichment as a technique for recovering microbes that could do almost anything and Avery's preoccupation with the capsule of the pneumococcus and its role in virulence. René brashly stated that it should be easy to find an organism that could make a capsule-destroying enzyme, a statement that impressed Avery.

In the summer of 1927, without a job or definite plans, René was France's official delegate at the First International

Congress of Soil Science in Washington, D.C. Along with 275 soil scientists from all over the world, he traveled throughout the United States and Canada in a chartered train to visit agricultural experiment stations and to examine different soil formations. He was offered at least two jobs that summer, one at the Experiment Station in Fargo, North Dakota, and the other at The Rockefeller with Avery—at half the Fargo salary—which he readily accepted. A series of accidental events had finally led him to a place where he could immerse himself in activities favorable to the development of his remarkable career.

Dubos's laboratory career can be divided into three general phases. The microbiology period, from 1927 to 1944, was devoted to demonstrating that bacteria nourished in the proper environment can produce enzymes specific to those bacteria and to showing that bacteria have genetic mechanisms. During the tuberculosis and experimental pathology period from 1944 to 1960, certain products of bacteria were shown to stimulate immunity, and environmental factors were found to influence susceptibility to disease. The environmental period, from 1961 to 1971, was dedicated to showing that various environmental stresses affect the development of the whole organism.

At no time was there a gap or significant change in the direction of his career. The fourth and final phase of his life, from his official retirement in 1971 until his death in 1982, was spent writing and lecturing on environmental and social determinants of health and disease. As he evolved into an environmentalist, he applied his earlier concerns to broader fields. His interests progressed from studies of pneumonia and tuberculosis to the whole pattern of disease and, finally, to the quality of human life on earth. The unifying thread in this seeming diversity was his perception that any living or ganism, whether microbe, man, or society, can be understood only in the context of the entire web of relationships it forms with everything else. A brief review of his major accomplishments in each of these phases reveals his continuous search for those factors in health that he believed are determined more by surroundings than by the mere presence or absence of microbes.

The microbiology period began with Dubos working alone in a small laboratory on the sixth floor of The Rockefeller Institute Hospital. Within three years, he succeeded in fulfilling the promise he had made to Avery: He recovered a microorganism that decomposed the capsule of Type III pneumococcus. He then proceeded to extract and purify the enzyme responsible for this activity, and finally he demonstrated that administration of the enzyme would protect rabbits or monkeys against usually fatal experimental pneumococcal infection. These impressive laboratory findings were described in several papers between 1930 and 1934. The enzyme might well have been further purified and then used to treat certain cases of pneumococcal pneumonia in humans, but the sulfa drugs had just become available for the treatment of this disease. The capsule-destroying enzyme did not achieve fame as a specific therapeutic agent, but the research on this material was nevertheless an auspicious beginning of Dubos's microbiological work.

In his search for a capsule-destroying microbe, René used the soil enrichment technique and added the capsular material to various soil samples. When he had isolated a suitable organism and maintained it in pure culture in the laboratory, he made the arresting discovery that the organism produced the capsule-destroying enzyme only if the capsular material were included as the sole source of carbohydrate in the culture medium. He called this phenomenon adaptive, or in duced, enzyme formation, which demonstrated that a cell has multiple potentialities that become manifest only when placed in an environment where it is compelled to use them.

René often referred to this discovery as the greatest intellectual satisfaction of his research career. The techniques in biochemistry and genetics to inquire further into this phenomenon were not yet available, but were later used by his friends Jacques Monod, François Jacob, and André Lwoff, who received the Nobel Prize for their work on this topic.

In the mid-1930s René and colleagues used the soil enrichment technique to isolate bacterial enzymes that destroyed creatinine and enzymes that converted creatine into creatinine. These materials were used to develop methods for measuring creatinine in the blood and urine, which had not been possible up to that time. In 1937 and 1938 he published papers on the recovery and partial purification of the enzyme that degraded one type of nucleic acid, and he named the enzyme ribonuclease. He did no further work with the enzyme, but it served as the basis for research by a number of scientists at The Rockefeller. Moses Kunitz further purified ribonuclease and obtained crystals of this protein. Stanford Moore and William H. Stein used the highly purified ribonuclease as material for their work on amino acid analysis of proteins, and Bruce Merrifield used ribonuclease in his first synthesis of an enzyme—discoveries for which these three men were awarded Nobel Prizes in chemistry.

Dubos's best known and most remarkable achievement during his microbiology period was the discovery of gramicidin and tyrocidin—the first antibiotics systematically cultivated from bacteria and produced commercially. Based on his several successes using soil as a source of special organisms, he searched for a microbe that would produce a substance capable of destroying intact bacteria. His search culminated in the isolation of *Bacillus brevis*, from which he extracted the active soluble principle he called tyrothricin that contains two substances that attack gram-positive organisms. Tyrocidin kills bacteria in vitro but not in vivo and is toxic to animals; gramicidin is active both in the test tube and in animals but is limited to external use (superficial wounds, bovine mastitis) because it causes hemolysis. Papers on these substances published between 1939 and 1941 established their structure, antibacterial activity, and clinical efficacy.

In this way, Dubos provided methods through which other antibiotics came to be discovered. His work stimulated Howard Florey and Ernst Chain to look further into Alexander Fleming's penicillin, which was found in 1928 but neither purified nor obtained in large enough quantities for testing. It also stimulated Waksman, René's former teacher, to undertake a search that led to streptomycin. Fleming, Florey, Chain, and Waksman subsequently received Nobel Prizes for their discoveries. Dubos's antibiotics are not the ones widely used for the treatment of bacterial infections, yet he was a true pioneer in the development of antibiotics—the most momentous development in the history of medical science.

By 1941, when René was barely forty, the publicity surrounding his discovery of tyrothricin had made him a famous man. In that year, he reached the highest rank, full member, at The Rockefeller Institute and was one of fifteen members elected to the National Academy of Sciences. He was not, however, carried away by the notion that antibiotics were wonder drugs that would eliminate all disease. In a 1942 article in the *Annual Review of Biochemistry*, he predicted that bacteria would adapt themselves to these drugs and that new strains would become resistant. Having opened the pathway for the discovery of antibiotics, he no longer found it intellectually challenging nor was he interested in devoting his life to finding more of them. He felt this type of research was more suitable for pharmaceutical laboratories.

The fifteen years of this microbiology period were, for the most part, happy and successful. In 1934 he married Marie-Louise Bonnet, a French teacher and pianist, and in 1938 he became an American citizen. He suffered a third episode of rheumatic fever, however, following a severe streptococcal infection. In 1940—under the stress of family problems related to world War II—his wife developed pulmonary tuberculosis, a reactivation of a childhood infection. Her condition grew progressively worse, and René, hoping that she would benefit from a change of environment, accepted a professorship at Harvard Medical School. But Marie-Louise died in the spring of 1942, and René went to Boston suffering from the severe emotional shock of her death.

As George Fabyan Professor of Comparative Pathology and Tropical Medicine at Harvard from 1942 to 1944, René had minimal teaching and administrative responsibilities and could concentrate on research. His letter of acceptance stated his wish to study the physiology and immunology of the tubercle bacillus and tuberculosis infection—an investigation stimulated by the illness and death of his wife. The critical wartime need for tropical medicine research, however, led René to work on the problem of bacillary dysentery.

While in Boston, the Lowell Institute invited him to deliver a series of public lectures on science. The lectures were published as his first book, *The Bacterial Cell in Its Relation to Problems of Virulence, Immunity, and Chemotherapy* (1945). Written in a somewhat philosophical manner (perhaps a reflection of the intellectual atmosphere at Harvard), this classic text reviewed the biochemistry and variability of bacteria and analyzed the mechanisms of pathogenesis in terms of individual components of the bacterial cell.

Despite many invigorating friendships and pleasant social occasions, René was lonely, and Boston became linked in his mind with the loss of his wife. When Thomas Rivers and

Herbert Gasser asked him to return to The Rockefeller in 1944 to head his own laboratory once again, he readily accepted and came back to begin work on tuberculosis.

Dubos's work during his tuberculosis period was not limited to microbiology but included experimental pathology and even clinical studies. René began with the conviction that tuberculosis became an important social disease only under certain social conditions, and he decided to work both on the chemical nature of the virulence of the organism and the social determinants of the disease. Between 1945 and 1960, several outstanding junior and senior colleagues did notable work in the Dubos laboratory. One colleague deserves special mention—Jean Porter, the technician who returned with his staff from Harvard and became his wife in 1946.*

The first major advance in the Dubos lab was a technical one—the introduction of nontoxic wetting agents into the culture medium to enable diffuse growth of tubercle bacilli. Previous research in the field had been hampered by the fact that these organisms were very slow-growing and could be cultured only as a surface pellicle, making quantitation impossible. The new technique brought about a renaissance in tuberculosis laboratory research. Several of Dubos's papers describe the use of these wetting agents (specifically the detergent Tween) and other factors—such as albumin and fatty acids—that led to vigorous, dispersed growth of tubercle bacilli. This advance in culture method enabled researchers to make accurate, quantitative studies of various strains of tubercle bacilli and of their virulence and pathogenic properties, for the first time. The Dubos laboratory could then investigate both host and microbe responses to a number of variables that constituted stresses. They produced an impressive stream of publications between 1948 and 1955 on

* Mrs. Jean Dubos died on August 6, 1988.

such topics as the virulence and immunizing properties of various attenuated BCG strains, the effect of diet on the course of experimental tuberculosis in laboratory animals, and the nature of some tissue substances that inhibited the growth of tubercle bacilli.

In the mid-1950s, Dubos's laboratory work in tuberculosis was supplemented to include human clinical studies done in a special unit of The Rockefeller Institute Hospital. By this time, effective chemotherapy for tuberculosis was available, and the clinical studies were designed to determine whether or not traditional treatment, with prolonged bed rest, was still necessary in patients receiving optimal medications. The findings indicated that prolonged bed rest was not needed. While the tuberculosis clinicians initially were reluctant to accept this result, it was confirmed—and led to the closing of tuberculosis sanitaria, marking the end of an era in the annals of medicine.

This period of clinical studies was particularly exciting for René, who had a special respect for physicians. He was at times a frustrated Ph.D. among the many M.D.s at The Rockefeller. With the tuberculosis project, however, he helped physicians read chest X rays and plan protocols for tuberculosis patients. Most of all, he enjoyed putting on a white coat and joining rounds on the ward to show concern for "his patients."

It was during this period that René began the transition from laboratory scientist to environmentalist. His reference book for physicians and medical students, *Bacterial and Mycotic Infections of Man* (1948), hinted at this shift, stressing as it did the *process* of infectious diseases. In his biography of Louis Pasteur (1950), he turned toward the social and historical study of disease, analyzing his hero's contributions to microbiology in the context of nineteenth century scientific thought—an intellectual life that, in many ways, paralleled his own. This book was written during his wife Jean's convalescence from tuberculosis. After her recovery, they collaborated on a multidimensional study of this disease, *The White Plague—Tuberculosis, Man, and Society* (1952). Extrapolating from their laboratory studies and using illustrations from medical, social, and literary history, they enlarged the theory that susceptibility to infection was closely related to environmental disturbances.

The key book resulting from Dubos's thoughts about illness, and his most popular work, was *Mirage of Health* (1959). Embodied in its title is his ecological view that man will never be free from disease because he must continuously adapt to environments in flux: Disease results from the dynamic process of life. In *Dreams of Reason* (1961), he questioned overconfidence in science's ability to eliminate disease, advocating, instead, using the means and knowledge of science to determine the kind of health society wants. A more explicit, scientific statement of his views on environmental biomedicine appeared a few years later in *Man Adapting* (1965), which emphasized that states of health or disease are organisms' adaptive responses to environmental challenges. Public response to these writings ensured Dubos a continuous flow of invitations to lecture all over the country on environmental aspects of health and disease.

The last ten years of René's laboratory activity in environmental biomedicine was an outgrowth of the tuberculosis work that incorporated some of his emerging convictions about what causes disease. He conducted studies on the influence of metabolic factors, nutrition, and environmental stresses on host resistance to various infectious diseases. Further bacteriological studies focused on the effects of environmental factors on the composition of normal gastrointestinal flora and its consequences on the host's development and resistance to disease. A final series of papers described lasting biological effects in newborn mice of early influences on their subsequent development, health, and longevity.

René's "official" retirement years were active ones. In the late 1960s, his prominent role in studying social and environmental effects on health brought him into the mainstream of the environmental movement. His highly publicized view that every part of life is interconnected made him a spokesman for those disturbed about the effects of a rapidly expanding technology on human life. René's eloquence in speaking and writing, coupled with his stature as a scientist, enabled him to bring these issues to the attention of a wide public audience. The well-deserved fame of his final years resulted from his passionate involvement in serving as the "conscience of the environment."

René presented his initial warnings on the health of the earth in *So Human an Animal* (1968), for which he received the Pulitzer Prize. He cautioned that humans are so well adjusted to their surroundings that they no longer mind the stench of automobile exhausts, ugly urban sprawl, "starless skies, treeless avenues, shapeless buildings, tasteless bread, joyless celebrations." He further warned that man's ability to adapt unconsciously to environmental threats means that basic human values will inevitably be destroyed. The book inspired concerned citizens with ideas and motivations for intelligent social action to combat environmental problems. René soon recognized, however, that the movement's zeal was misplaced, turning into a negativism that emphasized desecration and extinction. He changed his approach from provoking awareness of environmental perils to helping the movement develop what he believed they needed to survive: a philosophy of man in his environment.

In many lectures, articles, and books, René created this philosophy, using earthy terms and experiences of daily life to show that humans can act to shape their own destiny through their manipulations of the environment. This philosophy was based on his conviction that environments and institutions can never be better or worse than the individuals who shape them. *A God Within* (1972) emphasized the importance of developing the distinctive genius of each place, person, and social group, which in turn gives rise to richness and diversity in life. A complementary global attitude appeared simultaneously in *Only One Earth* (1972), written with economist and political scientist Barbara Ward, which served as the unofficial scientific and social guidelines for the First United Nations Conference on the Human Environment.

Beast or Angel? (1974) focused on the difficult choices and creative interventions into nature that humans must make to shape their ways of life, environments, and ultimately their civilizations. *The Wooing of Earth* (1980) presented a balanced primer: Man can improve on nature and even remove environmental degradation through deliberate social action, and the responsible use of scientific knowledge and technology are invaluable to these pursuits. His "Think globally and act locally" became the slogan of environmental activists and is still frequently quoted. His final book, *Celebrations of Life* (1981), amplified his equally well-known dictum that "wherever human beings are involved, trend is not destiny."

René's human-centered views, considerate of both liberals and conservatives in the environmental movement, continue to point the way to policies and solutions acceptable to all. His contributions to a philosophy of the environment can best be summed up in the title he gave himself and his regular column in *The American Scholar* (1970-1980). As a "Despairing Optimist," he lamented the deterioration of human and natural values; nevertheless he persisted in robust expressions of faith in the resiliency of nature and what he called the "creative adaptations" of mankind.

René Dubos achieved worldwide fame as a microbiologist, experimental pathologist, author, lecturer, and environmentalist—any one of which would have sufficed as a successful career. Despite the unfavorable prognoses of his childhood illnesses, he lived a long and productive life, remaining vigorous until his death at eighty-one. He was endowed with many intellectual talents, great sensitivity, originality, and rigorous self-discipline. His contagious enthusiasm for new ventures and his endless curiosity and wonder about life were especially important for achieving so many goals.

Those of us who knew René as a friend recall personal habits and strengths the public man did not reveal. The outward manifestations of his life were plain and simple, sheltering an intense dedication to his work. Every day, just before 9 A.M., he walked the few blocks from his New York apartment to the laboratory at 66th Street and York Avenue. As soon as he reached his office, he shed his suit jacket for a beige laboratory coat. During the active years he went directly to the lab bench, eager to record overnight results, review protocols, and begin the day's experiments. When he no longer had the pressure of a lab, and writing and lecturing were important activities, he would sit down at his desk and begin to recopy and revise the innumerable pages he had written into the late hours of the preceding night. Writing did not come easily to him, and every manuscript went through many handwritten drafts.

He took numerous rests from his reading and writing throughout the day and would engage one of us in long, involved conversations. These exchanges played a deliberate role in his work, for he used them to reformulate ideas he was struggling with on paper or he indulged in hypotheses, sometimes intentionally extravagant, about ideas he had just read. As we participated in his exacting disciplines of learning, thinking, and writing, we in turn gleaned much from his insights and observations.

Sharing a Rockefeller lunchroom table with René was an exciting and unpredictable experience. There he led discussions on the latest scientific news or, more ardently, on the unusual profusion of interests he had outside the lab. Whether it was growing truffles in the laboratory, infections that produced beautiful variegated tulips, or why water does not freeze in fire hydrants in the winter, he enlivened every meal with remarks and stories that made his company a delight. René also served as editor of *The Journal of Experimental Medicine* from 1946 to 1972 and participated in journal club and lecture activities at The Rockefeller. He did not indulge in sports, clubs, hobbies, or other extracurricular activities, but could be the life of a party on the infrequent occasions when he allowed himself to participate. Like Avery, he avoided much of the busy-ness of science, spending countless hours in thinking and debating what he felt was really important about the countless things that could be done.

Outside the laboratory, René's most enjoyable moments were spent quietly with Jean. In the later years, he would leave The Rockefeller promptly at 5 P.M. and walk briskly home where more discussions, reading, and writing continued late into the night. His travels and lectures were arranged so that he and Jean could spend weekends on their Hudson Highland property in Garrison, New York. René was particularly fond of planting and pruning trees, clearing brush to make trails through hemlock groves, observing the resident frogs and turtles, or tending a small vegetable garden—all the while meditating on his own interventions into nature. It is no surprise that his best writing took shape in these invigorating surroundings.

René Dubos was a scientist in his respect for facts and his exacting requirements for evidence. He was drawn naturally to humanism through his tireless efforts to reconcile man's biological uniformity with his social diversity. His emphasis on the interplay between living things and their environment made him conceptualize an area of medical science that is only now beginning to grow. He contributed to a philosophy of scientific humanism by perceiving that all forms of life on earth are integrated components. René will be remembered for formulating broad questions affecting human life, many of which are not yet ripe for solution. Fortunately, his extensive legacy of books and essays will continue to provide perceptive counsel for generations to come.

HONORS AND DISTINCTIONS

Awards And Memberships

1940 John Phillips Memorial Award, American College of Physicians
1941 E. Mead Johnson Award, American Academy of Pediatrics
1945 Member, National Academy of Sciences
1945 Member, The Century Association
1946 Gordon Wilson Medal, American Clinical and Climatological Association
1948 Lasker Award, American Public Health Association
1948 Member, Practitioners' Society, New York City
1950 Member, Academia de Ciencias Fisicas, Matematicas, y Naturales, Venezuela
1951 Trudeau Medal, National Tuberculosis Association
1954 Member, American Philosophical Society
1958 Howard Taylor Ricketts Prize, University of Chicago
1960 Fellow, American Academy of Arts and Sciences
1960 Passano Foundation Award
1960 Robert Koch Medal, Robert Koch Foundation, Berlin
1963 Phi Beta Kappa Award in Science for *The Unseen World*
1965 Phi Beta Kappa Award in Science for *Man Adapting*
1966 Arches of Science Award, Pacific Science Center
1968 Two Cultures Award, Flushing High School, New York City
1969 Pulitzer Prize for Nonfiction for *So Human an Animal*
1969 Benjamin Franklin Fellow, Royal Society of Arts
1970 Harold Terry Clark Medal, Cleveland Museum of Natural History
1972 Frances K. Hutchinson Medal, Garden Club of America
1972 Prix de l'Institut de la Vie, Paris
1973 Bradford Washburn Award, Boston Museum of Science
1975 Cullum Geographical Medal, American Geographic Society
1976 Tyler Ecology Award, Pepperdine University
1979 Wilder Penfield Award, Vanier Institute of the Family
1979 Member, American Academy and Institute of Arts and Letters

Honorary Degrees

Forty-one honorary degrees, including three honorary doctorates of medicine, from thirty American and eleven foreign institutions, 1941 through 1981

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John Ray Dunning

September 24, 1907-August 25, 1975

By Herbert L. Anderson

John Ray Dunning, professor of physics at Columbia University, was a pioneer in the development of nuclear energy. From 1932, when he was twenty-five, he worked almost exclusively on the study of the then newly discovered neutron. His work led naturally to the demonstration—the first in the United States—of the large release of energy in the fission of uranium by slow neutron bombardment.

Dunning realized that by enriching uranium in the light isotope, he could make a nuclear chain reaction a practicality. His work to adapt the gaseous diffusion process for this purpose made possible the nuclear power industry as we know it today. This achievement, pursued with unique vigor and single-mindedness, places him in the ranks of outstanding scientists of this century.

After leaving active research, Dunning served with great distinction as dean of the School of Engineering at Columbia, obtaining financial support for many scientific projects.

FAMILY BACKGROUND

John Ray Dunning was born in Shelby, Nebraska, the son of Albert Chester and Josephine (Thelen) Dunning, on September 24, 1907. His father was —according to Dunning himself, quoted in *Current Biography* , 1948—a "congenial, en ergetic, and hearty grain dealer." He was also an amateur radio engineer. John's early conviction that it was "easier to make equipment work ... than to save souls or prepare legal briefs" turned him away from the ministry and the law and led him to science. He was only twelve years old when he built and then operated a radio sending set, the first in his section of the country. After graduating from Shelby High School in 1925, he entered Nebraska Wesleyan University, and, in 1929, received a B.A. degree with highest honors. Between 1926 and 1929, he and his father, with the encouragement and assistance of one of his professors, built the radio stations WCAJ and KGBY, which operated on the regular broadcast bands and were later sold. Immediately after graduation, Dunning went to Columbia University, where he was an assistant in the physics department for three years and a university fellow from 1932 to 1933.

Dunning was married in 1930 to Esther Laura Blevins, now dead, who was his devoted companion throughout his lifetime. He was elected to the National Academy of Sciences in 1948. He died of a heart attack at his home in Key Biscayne, Florida, on August 23, 1975. He was sixty-seven years old. Two children, John Ray, Jr., and Ann Adele (the former Mrs. Edward Coyle), and a grandchild survive.

NEUTRON RESEARCH

The neutron, discovered shortly after Dunning arrived at Columbia, became his principal subject of research. This work was supported enthusiastically by George B. Pegram, who had resigned his post as dean of engineering to do research. Their collaboration was both close and productive, and they published twenty-four papers together on neutrons between 1933 and 1936. Dunning's drive and exceptional skill "in making things work" contributed greatly to their joint success. One 1934 paper, "The Emission and Scattering of Neutrons," became the basis of his Ph.D. dissertation.

Dunning spent his entire career at Columbia. He was appointed to the faculty as an instructor in 1933, received his Ph.D. in 1934, and advanced to assistant professor in the following year. He became associate professor in 1938 and professor in 1946.

Granted a Cutting Traveling Fellowship in 1936, Dunning traveled extensively in Europe, taking advantage of the opportunity to meet with many distinguished physicists—among them Rutherford, Chadwick, Bohr, Heisenberg, and Fermi—to discuss his work on neutrons.

After his 1935 promotion to assistant professor, Dunning became the central figure in neutron research at Columbia. His was the leading laboratory for neutron research in the United States, complementing Fermi's laboratory in Rome. Segrè, Amaldi, Rasetti, and Fermi himself came to Columbia to work with Dunning and his colleagues. He also worked with a procession of graduate students and younger faculty members, studying, among other topics, the magnetic properties and magnetic moment of the neutron. One experiment of fundamental importance, the scattering of neutrons by ortho- and para-hydrogen, was done in collaboration with a group from the National Bureau of Standards.

PERSONALITY

What kind of a man was John Dunning? As one of his former graduate students, William W. Havens, Jr., put it:

> Dunning was a man of contagious optimism, boundless enthusiasm, and almost infinite energy. He was also an inspired experimentalist who knew intuitively the critical factors in a scientific problem. He had a real flair for getting apparatus to work. On many occasions, his graduate students would give up in despair when one of Dunning's electronic devices would not function. Dunning could then be found in the laboratory at 2:00 or

> 3:00 A.M. fiddling with the apparatus and by dawn it was usually working perfectly. His colleagues jokingly referred to the 'DOF' or 'Dunning Optimism Factor' when planning any project because Dunning always minimized the difficulties and emphasized the accomplishments. However, all admired the ingenuity, enthusiasm, and inspiration he contributed to any project.

My own view is very much in accord with this. Dunning had a deep conviction that, unless fundamental principles were being violated, the apparatus had to work. It was just a matter of getting it to do what it was supposed to do anyway.

CYCLOTRON

In the early days, before accelerators were common, a mixture of beryllium powder and radon gas contained in a small glass bulb was used as a neutron source. Such sources had a yield of 106 neutrons per second. The radon was obtained from Memorial Hospital by "milking" four grams of radium every few days for this decay product (half-life = 3.8 days). The radon was used primarily in gold seeds for implantation in cancerous tumors, but there was plenty available for the neutron work.

Still, Dunning followed the news of Ernest Lawrence's successful development of the cyclotron at Berkeley with great interest. He wanted a much more powerful neutron source than he had at his disposal, and the cyclotron was the way to go. When he heard of an 80-ton magnet like that Lawrence had used in the construction of his 37-inch cyclotron, he went after it. These magnets had been produced by the Federal Telegraph Company during World War I to be used in Poulsen arc generators, a type of radio transmission that became obsolete after the invention of the vacuum tube.

In the 1930s, no government funds were available for such a project and universities measured their budgets for research in the hundreds of dollars. But Dunning was un daunted. His energy, enthusiasm, and self-confidence were persuasive, and he went around raising money from foundations and obtaining gifts of equipment from industry until the magnet was shipped and installed and a cyclotron built in the basement of the Pupin Physics Laboratory at Columbia.

Dunning worked with a small staff. Dr. E. T. Booth, his long-time collaborator and a postdoctoral fellow at the time, worked full time constructing the cyclotron and getting it to work. My own recollections are vivid of Booth, infinitely patient, looking for leaks. As a graduate student hoping to do my thesis experiment with the cyclotron, I was assigned a variety of tasks. Hugh Glassford, an engineer, looked after the more conventional engineering needs. Three junior members of the faculty, G. N. Glasoe, D. P. Mitchell, and Hugh Paxton worked on the cyclotron part time.

Once built, the cyclotron was a huge success. It played a crucial role in the development of nuclear energy and is now on permanent exhibit at the Smithsonian Institution in Washington, D.C.

FISSION OF URANIUM

When fission was discovered in 1938, Dunning was the right man at the right place at the right time. He had a strong source of neutrons from his cyclotron. He had constructed a linear amplifier-ionization combination that could be readily adapted to detect the large energy release expected from the fission of uranium. Moreover, he had a great deal of experience with neutrons, especially slow neutrons.

It is important to point out that the idea of looking for the energy release in fission was attributable to Otto Frisch and his aunt, Lise Meitner. Frisch was the first to realize that the fast-moving nuclei from the splitting of uranium would produce a huge amount of ionization compared with the background from the alpha particles of uranium decay. Frisch also had a uranium-lined ionization chamber connected to a linear amplifier and he readily saw huge pulses of ionization on an oscilloscope when a neutron source—300 milligrams of radium mixed with beryllium—was brought up to the ionization chamber. It was a historic occasion. Niels Bohr was at the point of leaving for the United States when Frisch came to report these results. Because of his concern about priority, Frisch asked Bohr not to mention these results to the Americans until the paper he was preparing about them appeared in print.

We have Dunning's own recollection of what happened at that time in a speech he gave to the American Physical Society some years later:

> On the morning of Wednesday, January 25, 1939, Willis Lamb, returning from Princeton where Professor Bohr was lecturing, brought further news of Bohr's analysis of Otto Hahn's brilliant chemical identification of lower atomic weight elements like barium in the products resulting from neutron capture by uranium, thus clearly suggesting splitting the uranium-plus-neutron system, rather than the transuranic series postulated before. In discussions around the [Columbia] faculty club lunch table it was clear that large kinetic energy release should accompany such splitting. Fermi, Rabi and others left for the Fifth Annual Washington Theoretical Physics Conference. After returning to the Pupin cyclotron laboratory, it seemed clear we should try to detect the energy, which on elementary mass-defect reasoning ought to be in 100 or 200 MEV range.
>
> Unfortunately, the new cyclotron in the Pupin basement was behaving poorly, and chamber modifications were being made by Dr. E. T. Booth, Dr. F. G. Slack, and Herbert Anderson, but I hoped it could get working that afternoon. A flexible new linear amplifier-ionization chamber-oscillograph system was already installed next to the cyclotron—being used largely as a neutron detector with the cyclotron. After several attempts a small metal disk was finally coated with uranium oxide and installed in the ion chamber as one electrode. The alpha-particle pulses around 4.5 MEV were clearly visible.
>
> That evening, while my colleagues still worked on the cyclotron, I fi

> nally brought from the thirteenth-floor laboratory a radon + beryllium fast neutron source—the type used for most of our previous work—and placed it next to the U-containing ion chamber. In great excitement, we saw about one big pulse on the oscilloscope every minute. The rate was so slow we had doubts at first whether it was real or maybe a poor electrical connection. But when I put the neutron source in a paraffin vessel, usually called a slow-neutron "howitzer," my notebooks indicate that the rate went up to seven or so huge pulses per minute. With a cadmium, slow-neutron-absorber screen interposed, the rate dropped to around one or two a minute. Clearly the main effect was due to slow neutrons. A rough calibration of the pulse height versus the 4.5 MEV alpha-particle pulse height indicated around 65 to 100 MEV peak energy. Since in fission, one of the two fragments goes backwards into the electrode plate, the total energy per splitting should be in the 130 to 200 MEV range. Fission energy was clearly a new order of magnitude!
>
> We quit about eleven P.M. My diary that night says cryptically: "Believe we have observed new phenomena of far-reaching consequences," and relates what I have just described.

In addition to Dunning's recollections, the archives of The University of Chicago library preserves a notebook containing my own first observations, as Dunning's graduate student, of fission pulses.

Two days later, Dunning sent a telegram to Fermi in Washington announcing these results. The opening talks by Bohr and Fermi at the Fifth Washington Conference on Theoretical Physics on January 26, 1939, about the implications of the chemical evidence for the fission of uranium obtained by Hahn and Strassmann were sensational. The physical evidence obtained by Frisch a few weeks earlier using the ionization method demonstrated the energy release. Dunning's result confirmed it and was quickly repeated in three other American laboratories. The implications for nuclear power and possibly nuclear explosives were immediately recognized and given wide media coverage. Dunning had helped open the nuclear age.

These results of the Columbia group plus some additional observations on the nature of the fission process were promptly reported in a classic paper in the March 1, 1939, issue of the *Physical Review* , "The Fission of Uranium," by H. L. Anderson, E. T. Booth, J. R. Dunning, E. Fermi, G. N. Glasoe, and F. G. Slack. Words alone cannot recapture the excitement of those times.

THE CHAIN REACTION

To make nuclear power and nuclear explosives practical, it was recognized that it would be necessary to induce large numbers of fissions using large quantities of uranium. This could be done if neutrons were emitted in the fission process. In this case, it would be necessary to arrange matters so that the new neutrons would cause additional fissions, with further additions from the neutrons from these in turn. With more neutrons produced than absorbed in each generation, there would be a rapid buildup in their number—a chain reaction.

In the late 1930s, there was, as yet, no evidence for the neutron emission. Moreover, the cross-section for fission by slow neutrons in natural uranium was rather small, raising the question of excessive loss of reproduction factor due to parasitic processes.

The question was how to proceed from there. The Columbia team split up. Fermi and Anderson decided to try to obtain a chain reaction using natural uranium and a suitable means for slowing down the neutrons. Dunning, Booth, and Slack—believing that the isotope responsible for the slow neutron fission was U^{235}—opted to enrich the uranium with this isotope by the gaseous diffusion method. This was the surest way to proceed provided the problem of isotope separation could be solved in a practical way. Dunning had no doubt it could be done.

LETTER TO NIER

He lost no time. If he could demonstrate experimentally what seemed plausible from the arguments of Bohr and Wheeler, then the proper course for nuclear energy was by enrichment of the light isotope U^{235}. On April 6, 1939, Dunning dispatched a letter to Alfred O. Nier, then a professor of physics at the University of Minnesota, to enlist his support in making this test. The letter shows how clearly Dunning understood what was involved. Because of its historic importance, I have reproduced the letter here in its entirety:

Dear Professor Nier:

> There are a number of things which I hope to be able to discuss with you during the Physical Society meeting in Washington, April 27-29. I trust you will be there as usual as I understand you have a paper.
>
> In order that you will be acquainted with the situation from my point of view so that you can consider the possibilities before we meet, perhaps the following should be outlined.
>
> The demonstration that uranium splits or fissions, particularly with slow neutrons, with very large energy evolution opens many far-reaching possibilities. It is now quite certain that the recoiling fragments emit some secondary neutrons. The fragments have too little positive nuclear charge for their atomic weight, i.e., they have a neutron excess and are unstable. They therefore achieve stability by emitting betas or neutrons or both. This is almost obvious. As a matter of fact Dr. Booth and I started looking for secondary neutrons almost immediately after demonstrating that U fissions the last part of January, although the first experiments were not very conclusive. Later experiments by a number of people here and abroad all indicate the existence of secondary neutrons. There are likely to be somewhere between 1 and 5 secondary neutrons per fission. Fermi is going into that phase of the problem particularly.
>
> If there is on the average at least more than one secondary neutron for each "primary" neutron, so that the net effect of the absorption of neutrons through non-fission processes is more than counterbalanced, then we have the possibility of setting up a self-perpetuating, cascade type of reaction analogous to ionization by impact build-up. The development

of enormous energy through the release of nuclear energy on a large scale is coming closer to realization than most people realize.

From simple physical reasoning, it seems clear, crudely speaking, that the following factors must be considered: On the one hand we have (A). Neutron fission processes: Concentration of fissioning U, together with the effective fission cross-section of the U; on the other hand (B). The summation of the non-fission capture processes: i.e., summation of the concentrations of the various capturing elements or isotopes in the system (including the U), each with its appropriate cross-section. In addition we have (C). The effective number of neutrons liberated per fission; and finally (D). The effective probability of a neutron to stay in the system, i.e., not to escape. (This is always less than 1).

Of course, this must be summed or integrated and the variables considered as functions of the neutron energies. So far as I know, no one has dealt with this problem on any thorough basis, and it is obvious that the exact calculations are going to be quite involved. However the essential physics is fairly simple and it seems that if (A/B)CD is effectively greater than unity, then a chain reaction will occur. (Ed note: The quantity (A/B) should be the fraction of neutron captures that lead to fission; thus, B should include the neutron capture processes that lead to fission.)

There are some very serious problems yet remaining however. The actual cross-section for fission with slow neutrons of uranium is not very large—only about 2 to 5 × 10^{-24} cm^2 at most, so the numerator A above is not large. Unfortunately, there is also a strong resonance capture of neutrons by U which almost certainly does not give fissions, and this gives a fairly high cross-section all through the slow neutron region as well as the sharp peak at resonance (or resonances). This competing process thus contributes to (B) above. In addition, there are other contributions to (B), inevitably, such as capturing elements in the material of construction or in slowing down media such as H_2-containing materials, or in various impurities such as boron or cadmium which will be especially bad. From what we know of the various cross-sections involved now, I believe there is virtually no safety margin left for a successful chain reaction system with ordinary uranium, certainly not unless extreme purity and special slowing down materials are used, possibly deuterium—ordinary water seems out (H absorption). Very large amounts of material will be required or else the neutron escape factor (D) will be serious. It is clear that making a chain reaction "go" is not going to be easy.

There is one line of attack that deserves strong effort, and that is where we need your cooperation. The important question is which uranium isotope is really responsible for slow neutron fission? It is a matter of opinion largely, and some theoretical physicists think one way, some think the other. Bohr thinks 235, but Fermi is neutral or inclined toward 238. Bethesda and Placzek are on opposite sides of the fence, in fact there is a bet on. It is of the utmost importance to get some uranium isotopes separated in enough quantities for a real test of the whole question.

If U^{235} can be shown to be the one responsible for the slow neutron fission, then it is very certain that the chain reaction can be produced, particularly if the U^{235} is concentrated some. Assuming your figures on the relative proportion in ordinary ores of about 1/140, this would raise the effective slow neutron cross-section from about 2 to 5 × 10^{-24} cm^2 for ordinary U, to about 275 to 700 × 10^{-24} cm^2 for pure U^{235} in the (A) term of the discussion above. This would be certain to work even with a very small secondary neutron excess over 1. It would also permit the presence of very much larger amounts of other capturing materials. Furthermore the sizes and amounts of materials required would be much reduced. Thus while the chain reaction may be made to go eventually with ordinary U, clearly if U^{235} is the one, we open a whole new realm of possibilities with a really concentrated energy source. Reasonably pure U^{235} probably will be explosive under some conditions, which may make a great military weapon of enormous power.

We are pushing up the cyclotron neutron output steadily. If you could effectively separate even tiny amounts of the two main isotopes, there is a good chance we could use very tiny samples to demonstrate which isotope is responsible, and study the whole phenomena. There is no other way to settle this business except to work with separated isotopes. Dr. Booth and I have the cyclotron and all the other necessary equipment and techniques. If we could all cooperate, and you aid by separating some samples, then we could by combining forces settle the whole matter.

There is a great opportunity here, as I'm sure you realize. I hope you will give serious consideration to what you could do to rebuild your spectrometer system for this purpose, and let us get together and discuss it all in Washington. It will not be necessary to make a complete separation. A compromise in between for quantity production is more important than resolution.

Sincerely yours,
John R. Dunning

Please excuse the typing—I did it myself.

P.S.

It cannot be overestimated how important this really is. I had already made a number of layouts of atomic energy systems, almost immediately last January. A considerable number of variations are possible depending on the choice of slowing down and neutron "reflector" materials, heat transfer materials (radical departures from standard heat engines are also envisioned—direct conversion). The secondary neutron emission, effective capture and the U^{235} concentration are vital, assuming we can demonstrate it in the face of all the theoretical arguments. (A sketch is given, not reproduced here.) This is only schematic but it shows that these ideas are practical, far more than physicists generally realize yet.

JRD

FISSION OF U^{235}

Some years later, as Dunning's diary recalls it:

Professor Nier eagerly accepted the challenge—building bigger special mass spectrometers, trying UF_6 as Dr. A. V. Grosse had arranged, then UBr_4—and finally, after many difficulties, on March 2, 1940, succeeded in sending us two tiny electrode sections labelled "U^{235} " and "U^{238}" with well under a microgram of U^{235}—quite invisible.
My notebook entry on March 2, 1940, says cryptically: "U^{235} + U^{238} samples from Nier received. Made from UBr_4. Demonstrated conclusively slow neutron fission due to U^{235}. Atomic energy released now definitely assured at last!! Some concentration may be desirable, but the new era can now be seen!
Large scale separation methods are clearly needed now conclusively; considering 1) electrical, 2) centrifugal, 3) thermal diffusion, 4) gas and liquid diffusion."

No time was lost in getting the means for separating the isotopes under way. The following excerpts from a speech by Eugene T. Booth as part of the memorial service for Dunning in 1975 tells the story and shows how Dunning's unique personality made it all possible:

> I remember as yesterday when John and I were returning from a trip to Schenectady—I believe it was in 1940. We had stopped for dinner, late in the evening, and reviewed again the various methods of separating isotopes. These were ruled out, one by one, as not suitable for use with uranium on a large scale, all except the gaseous diffusion methods. It was realized that new features would have to be devised, but fundamentally this approach appeared feasible.
>
> From that day on, separation of the isotopes of uranium by gaseous diffusion became an obsession with John, in the creative sense of the word. Nothing would daunt him. After many turbulent periods of uncertainty, the diffusion plants at Oak Ridge were constructed and are still operating today. Further expansion of capacity is being planned even now.

Booth goes on to quote a letter dated May 3, 1950, from General L. R. Groves, a man who dealt with Dunning during the war and was in a good position to evaluate his contribution to the Manhattan Project:

> . . . I did have personal contact with Professor Dunning during the Manhattan Project period, as well as since then. I am glad that you saw my letter to him of about four years ago, as I am sure that it expressed my views about his value to the Project—that is, insofar as they could be made public. As a matter of fact, Dr. Dunning was of even more value. There was, as he may have told you, a great deal of adverse opinion among many scientists, and even among the group at Columbia as to the possibility of our being able to make the gas diffusion process an operable affair.
>
> Despite the prophets of doom among the scientific leaders, with respect to this phase of our work, Dr. Dunning never varied in his optimistic attitude. He was a great bulwark to me, as we were proceeding against the very positive advice of many distinguished scientists.
>
> . . . My main impression of Dr. Dunning during the War was that he was a man who was so full of his subject that he could not stop talking about it. It was always difficult to break off conversations with him. It was difficult at times for me to get in a question edgewise, and particularly, to get the answer from the man in actual charge of the particular experiment, as Dr. Dunning always seemed to want to do all the talking. He was just so enthusiastic, he seemed to be bubbling over.
>
> . . . I feel very strongly that Dr. Dunning has not been appreciated by his country for his work on the Project, and primarily, he has not received

> the credit due him for his scientific anticipation or intuition and for his courage in standing up against the opinions of his fellow distinguished scientists.
> Few people have had such a prominent role in establishing a new and important industry on a world-wide scale. The nuclear power industry today assumes even greater importance in the public mind with the realization that fossil fuels will require supplementation in the years ahead.

As is well known, the first chain reaction was made with a graphite pile using ordinary uranium. Although it was not anticipated in the beginning, it turned out that a by-product of the reaction was Pu ^{239}, a new isotope with slow neutron fission characteristics like those of U^{235}. The reactors built at Hanford, Washington, using ordinary uranium, produced Pu^{239} in sufficient quantity to make the first nuclear explosion at Alamogordo, New Mexico. The electromagnetic method produced enough U^{235} for the Hiroshima bomb. The Nagasaki bomb used Pu^{239}.

Because of the difficulties encountered in the development of a practical diffusion membrane, the gaseous diffusion method did not come into its own in time to help end the war. Instead, the first chain reaction was made with ordinary uranium using a graphite pile—Fermi's method.

Dunning recalled those difficult times in a talk to the American Physical Society he gave some years later:

> Unfortunately, we could not convince the Uranium Committee that our U^{235} gas diffusion process should be supported by the government, so we had to carry on the development ourselves. Not until August 1941 did our success gain official support. Then the engineering of the first diffusion separation plant at Oak Ridge gradually got under way in 1942, to ultimate success.

Officially, Dunning became director of research, Division I, SAM Laboratories. "SAM" stood for "Substitute Alloy Materials," code name for Columbia's nuclear laboratory. The original development work for the gaseous diffusion process was carried out in this laboratory, but the large-scale engineering research and development was done by the M. W. Kellogg Company under the direction of Percival ("Dobie") C. Keith.

For the construction of the huge plants at Oak Ridge, a new company, the Kellex Company, was established. It was completely owned by Kellogg, and staffed with virtually the same officers. The Oak Ridge gaseous diffusion plant, K-25, was built and began operating in 1945. Subsequently, the Oak Ridge complex expanded through several major plant additions. During the Korean War, two additional gas diffusion plants were built at Paducah, Kentucky, and Portsmouth, Ohio. The Union Carbide Company was selected to operate the first two, and the Goodyear Group the third. Dunning maintained close contact with all these entities until the whole enterprise was successfully launched. At the peak of their operations, these plants consumed about 15 percent of the total electrical power produced in the United States.

Dunning could, quite rightfully, take pride in the fact that, increasingly, nuclear power plants were being built using enriched U^{235} for their successful economic design and operation. In 1971, the pioneering work of Dunning and his three colleagues on the gaseous diffusion method for U235 separation was recognized by an award of $30,000 each, in lieu of patent royalties, by the Atomic Energy Commission. The work had been recognized as patentable by the U.S. Patent Office, but a patent could not be issued because of the secrecy restrictions.

NEVIS CYCLOTRON

After the end of World War II, Dunning served as scientific director for construction of Columbia's Nevis Laboratories, a cooperative endeavor of Columbia University, the Atomic Energy Commission, and the Office of Naval Re search. The principal activity was the construction and operation of the 385 MEV synchrocyclotron. The detailed design and construction as well as much of the initial operation was carried out by Dunning's close collaborator, Eugene T. Booth.

DEAN OF ENGINEERING

In 1946, Dunning was appointed Thayer Lindsley Professor of Applied Science, and in 1950, dean of the School of Engineering and Applied Science—appointments which marked the end of his active participation in research.

After his appointment as dean, Dunning threw himself into a fund-raising campaign that resulted in the construction of the Seeley Wintersmith Mudd and Terrace Engineering Center at Columbia. When he resigned his deanship in 1969, he had raised more than $50 million for the school.

He held numerous posts in the world of American science, including: member of the National Academy of Sciences, elected 1948; member of the board, American Association for the Advancement of Science; trustee, Fund for Peaceful Atomic Development; chairman, New York City Board of Education Advisory Committee on Science Manpower; member, Scientific Advisory Committee, Department of Defense; chairman, Science Advisory Council to the Legislature of the State of New York; chairman, President's Committee on Super-Sonic Transport.

In the 1950s, President Dwight D. Eisenhower and Admiral Hyman G. Rickover consulted him frequently on military matters and on the development of nuclear-powered submarines.

He was a member of the board of directors of a number of corporations and chairman of several. He received nine honorary degrees and eight awards.

MEDAL OF MERIT

President Harry S. Truman signed the citation accompanying the 1946 Medal of Merit. It reads as follows:

> Dr. John Ray Dunning for exceptionally meritorious conduct in the performance of outstanding service to the War Department, in accomplishments involving great responsibility and scientific distinction in connection with the development of the greatest military weapon of all time, the atomic bomb. As a physical researcher, he took a leading part in the initiation of the early phases of the project; then he was in charge of essential research in the SAM Laboratories for the Manhattan Engineer District, Army Service Forces, and then he served as advisor to the contractor for full scale operation of his process. A physicist of national distinction, Dr. Dunning's unselfish and unswerving devotion to duty have contributed significantly to the success of the Atomic Bomb project.

PUBLIC SERVICE

A strong believer in informing the public more fully about the nature and implications of atomic energy, Dunning spoke often across the nation before teachers' associations, business conferences, civic clubs, town meetings, as well as on radio and TV programs. These talks ranged over a broad spectrum of subjects: "Education for the Atomic Age," "On the Edge of Disaster—Technological Challenge to America," "On Science Teaching," "The What and How of Nuclear Power," "Sputniks Are Not Enough," "Breakthroughs in Science," "The Next 100 Years," and "Impact—Government Support and Engineering Education."

He took a special interest in explaining abstruse subjects such as nuclear fission to nontechnical audiences, with the aid of contemporary "props" whenever possible. For example, to help explain the principles of nuclear fission to youngsters of school age, he assisted in the production of a "Blondie and Dagwood" comic book that reduced the story of atomic energy to its simplest terms.

Similarly, he enlivened the Columbia Engineering dean's platform talks with a variety of mechanical and electronic gadgets he used to illustrate or dramatize his remarks. These included a radioactive "atomic ray gun"—inspired by Buck Rodgers's famous "disintegrator pistol"—Geiger counters, oscillographs, and various combinations of bells and colored lights that culminated in an "atomic pinball machine"—a miniature atomic power system that demonstrated actual atomic fission energy release.

For Dunning, the phenomenon of radioactivity never lost its fascination. I remember vividly the way he demonstrated the circulation of the blood using radioactivity. He prepared a sample of Na^{24} (15-hour half-life) by irradiating a glass of salt water with the cyclotron. Using a Geiger counter, he first showed that the radioactivity was in the glass. He then stretched out his hand with the Geiger counter at his finger tips: no activity. He then drank the glass of irradiated water. After some anxious minutes, the Geiger counter at the finger tips began to respond—at first weakly—then increasingly, as the circulating blood brought more and more of the radioactive salt to the finger tips. It was a great show. The audience loved it, and so did Dunning.

I wish to thank Professor Dunning's son, John Ray Dunning, Jr., for sending me the Nier letter and the Booth commentary extensively quoted here.

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California Institute of Technology

Arie Jan Haagen-Smit

December 22, 1900-March 18, 1977

By James Bonner

Arie Jan Haagen-Smit was born December 22, 1900, in Utrecht, a city in west central Holland. His father was the chief chemist of the Netherlands Royal Mint. The mint made gold and silver coins, and Arie's first chemistry lesson consisted of playing hide-and-seek with his sisters among piles of gold and silver bricks at the mint. He also had the opportunity to watch his father dissolve gold and silver coins to analyze them for their gold, silver, and copper content. But Arie's interest in chemistry was not aroused; he found the chemistry of gold and silver quite dull.

In high school, Arie became enthusiastic about mathematics. He taught himself calculus and found physics fascinating. He also became intrigued with languages, which he learned easily and found rewarding. In addition to English, he studied French, German, and Latin. His only poor grade in high school was in the Dutch language, and his wife, Zus, tells us that Arie was always a poor speller in Dutch.

During his high school days he also developed athletic skills. He became a rower and would begin rowing as soon as the canal ice melted in the spring. He also sailed on the lakes of Holland and was a champion boxer. Between rowing and boxing, he developed the largest biceps of any faculty member in the California Institute of Technology Division of Biol ogy up to about 1960. After 1960, when he gained worldwide recognition for his outstanding work on air pollution, he always wore a coat with sleeves and it was no longer possible to check on the status of his biceps.

In 1918, Arie entered the University of Utrecht and chose chemistry as his major. His wife believes that he might have become a mathematician or a physicist were it not for the fact that he was counseled by university officials that no positions were available in these fields in Holland. He studied chemistry as an undergraduate with a minor in mathematics. (As my mother used to tell me, a little chemistry can do no harm, and I sympathized with Haagy. I also had a chemistry undergraduate degree with a minor in mathematics.)

When the time came for graduate school, Arie again chose Utrecht and organic chemistry, considering inorganic chemistry a dull "assembly of facts." His organic chemistry professor at Utrecht at that time was P. van Romburgh, a natural products chemist who soon had Arie isolating a dermatitis-inducing agent from the outer layers (arils) of the fruit of the cashew nut. The cashews, imported from Java, were exotic and made Arie feel that he was studying the world. The agent from the arils, which became the subject of Arie's first published paper, turned out to be a substance closely related to the dermatitis-inducing agents of poison oak and poison ivy, not surprising in that poison oak, poison ivy, and the cashew nut are all species of the same family and therefore closely related.

Van Romburgh retired in 1928 and was succeeded by the young Leopold Ruzicka, fresh from Zürich. Ruzicka, then the young giant of European organic chemistry, was totally immersed in the study of the isoprenoids, in particular, the isolation, structure, and synthesis of the sesquiterpenes. Arie's work with Ruzicka resulted in his thesis, *Investigations in the Field of Sesquiterpenes*. This work awakened in Arie a lifelong interest in the chemistry of the terpenes, from the lowliest isoprene to polyterpenes such as rubber.

Arie received his Ph.D. from the University of Utrecht in 1929 and stayed on as chief assistant in organic chemistry. In this position, which has no exact correlative in American chemistry departments, he was able to do his own research on natural products but was also obliged to supervise undergraduate laboratory courses. It was an enviable position, but poorly paid.

In 1930, Leopold Ruzicka was called back to Zürich to become professor of organic chemistry at the Swiss Federal Institute of Technology. He was immediately succeeded at Utrecht by Fritz Kögel, a German who brought with him his assistant, Hanni Erxleben. Arie stayed on as chief assistant.

Utrecht at that time was the world center for the study of plant hormones. Caltech, which eventually numbered three Utrecht graduates among its chemistry faculty, was basically a substation of Utrecht for plant growth hormone studies and the only center for plant hormone study in the United States.

While still a Utrecht graduate student, Frits Went developed a biological assay for the plant-growth substance. Kögel, with Arie's assistance, set out to isolate the active principle, the plant-growth substance.

In 1954, Arie isolated this active material—then called heteroauxin, now auxin. The work, published that same year, established indole-3-acetic acid as a plant-growth material with auxin activity.

The isolation of this material laid the cornerstone of our knowledge of plant-growth regulation. In 1935, Kenneth V. Thimann at Caltech independently isolated indole-3-acetic acid from a different source. Where Arie had used human urine, Thimann used culture medium from the fungus *Rhizopus*—but the substance was the same. Indole-3-acetic acid was not isolated from higher plants and shown to be a hormone until 1946, but the effects of Arie Jan Haagen-Smit's findings about the chemical nature of the plant-growth regulator spread wide long before the compound was established as a natural plant component.

Arie never claimed special credit for this great discovery. Neither did he claim credit for an even more important find, made in the summer of 1935. Frits Went, then a faculty member at Caltech, spent that summer in Utrecht working with Arie. They discovered that substances never found in nature but chemically similar to indole-3-acetic acid, such as alpha-naphthalene-acetic acid, can mimic completely the action of indoleacetic acid in the control of plant growth. From this discovery—not patented by the discoverers—grew the whole field of chemical control of plant growth, the invention of 2,4-D as a weed killer, the idea of selective herbicides, the whole field of agricultural chemicals, and a multibillion-dollar business worldwide. This 1935 finding was monumental, its importance documentable only many years after the fact.

Meanwhile, work in Utrecht on the plant-growth hormone took a curious twist. The Went bioassay for auxin activity is highly specific for the natural hormone or closely related derivatives. In a series of papers published in Hoppe-Seyler's *Zeitschrift für physicalische Chemie* in 1933 and 1934, Kögel, Haagen-Smit, and Erxleben described the isolation in pure form and the structure determination of two active plant hormones, auxin a and b.[1] Auxin was revealed to be a

[1] These investigations took place from 1931 to 1936. From 1934 to 1935, I was a postdoctoral fellow in the Department of Chemistry at the University of Utrecht. I got to know Haagen-Smit, Kögel, and Erxleben very well. Erxleben was responsible for chemical degradations and structure determination, Haagen-Smit for isolation and biological assays, and Kögel for overall master planning, writing, and publication. So far as I know, Haagen-Smit had nothing, or next to nothing, to do with the chemistry or structure determination of auxin a and b.

trihydroxymonocarboxylic acid of eighteen carbon atoms. Auxin b contained one less carbon atom and one hydroxyl group, as well as one carbonyl group. Auxin a was isolated from human urine; auxin a and b were isolated from corn oil. (Only a single sample, from Hungary, contained the two hormones. All subsequent corn oil samples were free of both auxin a and b.)

Though it was later possible to obtain degradation products and determine their structure, the isolation of auxins a and b could never be repeated and turned out to be a scam perpetrated by Hanni Erxleben. Erxleben left detailed notebooks in which samples were properly recorded. After the end of World War II, J. A. Vliegenthart, the new professor of organic chemistry, reinvestigated these samples by mass spectrometry.[2]

"Authentic" auxin a turned out to be cholic acid; similar findings were made with respect to the degradation products. It is now believed that auxins a and b never existed. Haagen-Smit writes, "It is possible that the initial mistake was to advertise the purity of auxin a prematurely. Professor Kögel's eagerness to publish and his dictatorial behavior possibly made it very difficult for Miss Erxleben to retract her error, although this could have been done quite readily in the early period. It was Erxleben's persistence in covering up which led to the unwitting involvement of many associates."[3]

In any event, Haagen-Smit did not worry greatly about auxin a. Initially, he believed it existed, and after his arrival at Caltech he established a factory to produce it. When this factory produced only indole-3-acetic acid with no sign of

[2] J. A. and J. F. G. Vliegenthart, "Reinvestigation of authentic samples of auxins a- and b-related products by mass spectrometry," Proceedings of the *Recueils des Travaux Chimique des Pays-Pas*, 85(1966): 1266-72.

[3] From W. P. Jacobs, *Plant Hormones and Plant Development* (London: Cambridge Univ. Press, 1979), p. 57.

auxin a, he isolated indole-3-acetic acid from plants and from urine and let it go at that.

Although Utrecht was the original center of plant hormone work, Caltech grew in importance with the appointment of Herman Dolk and Kenneth Thimann to the faculty in 1930. The plant hormone group was further enlarged by the appointment of Frits Went and Johannes van Overbeek. In 1935, Thimann left Caltech to establish a competing plant hormone center at Harvard, and he persuaded Haagen-Smit to come to Harvard for the 1936-1937 academic year. At Harvard, however, the chemistry faculty could not decide whether or not there was such a thing as biochemistry, although Thimann, with a Ph.D. in that subject, certainly tried to convince them. In 1937, with Harvard in doubt about the wisdom of appointing more biochemists, it was relatively easy for Frits Went and Thomas Hunt Morgan, the chairman of the Division of Biology at Caltech, to persuade Haagen-Smit to return to Caltech. Arie and his wife Marie (known to all as Zus), rapidly took root in Pasadena, where they raised their children—Maria, Margaret, and Johanna (today Maria Van Pelt, Margaret Daniel, and Johanna Demers), and a son, Jan, from Arie's first marriage.

CALIFORNIA INSTITUTE OF TECHNOLOGY

At Caltech Haagen-Smit undertook a variety of tasks to determine, by trial and error, which would interest him the most. With David Bonner he found that adenine was a leaf-growth factor for radish leaves. With this author and James English, he discovered that the wound hormone active on bean plants was 1-decene-1, dodecanoic acid. With Joseph Koepfli and Gorden Alles, he isolated the active principle of *Cannabis sativa* (marijuana). With Edward Tatum, he identified the chemical nature of the precursor of the *Drosophila* eye pigment, and with several of his students he attempted the reisolation of auxins from plant material—attempts that always resulted in the isolation of indole-3-acetic acid.

Terpenes, however, remained his greatest love. He investigated the leaf oil of the California bay tree, *Umbellularia californica*, whose principal component is umbellulone. He separated the terpenes of guayule leaf oil, *Parthenium argentatum*, and, with Nicholas Mirov of the U.S. Forest Genetic Station in Placerville, determined the composition of the turpentines of a wide variety of pine trees. Separating the components of the pine turpentines by fractional distillation, he remarked in later years how simple it all would have been if he had waited until gas chromatography had been invented. He wrote what became a classic chapter on the chemistry, origin, and function of essential oils in plants for Gunther's 1948 *The Essential Oils*.

From the late 1940s onward, Haagen-Smit undertook a massive program to determine the flavor components of the pineapple. Reports of his studies with Arthur Prater, Clara Deasy, and Justus Kirchner were published in a series of articles beginning in 1945. This work led in turn to investigations of the flavor components of wines, onions, and garlic. Haagen-Smit passed air over plants enclosed in translucent plastic chambers, collecting in a cold trap the volatile flavoring materials evaporated from the plants. Investigating the chemical nature of these volatiles—that is, the substances distilled off plants exposed to the heat of sunlight-he found that there were many, particularly terpenes, that were distilled out of leaves and wasted. In some cases, the amount of terpenes wasted through distillation by sunlight amounted to one-quarter or more of the total photosynthate of the plant.

Haagy had many graduate students, including two of my brothers, Walter and David. He was good with students, suggesting interesting projects for them to work on, giving helpful suggestions, and teaching a fascinating advanced class on the chemistry of natural products. This class was always well attended. One of Haagy's graduate students told me several years after his departure from Caltech that his notes on the course "Chemistry of Natural Products" contained more meat and information than his notes from any other class he had taken as a graduate student at the Institute.

In addition to sharing the academic burdens of teaching and supervising graduate students, Arie served as the Division of Biology's first executive officer, a position he held for six years. I remember there was so much work to do as executive officer at the time that each evening, instead of a briefcase, Arie took home a suitcase full of papers to work on. In the morning, he brought back the suitcase full of resolved work.

SMOG AND MICROCHEMISTRY

Until well into World War II, the gasoline produced in southern California was produced by the straight fractional distillation of crude oil and principally contained saturated hydrocarbons. In the summer of 1943 a butadiene plant for the manufacture of one monomer for a synthetic rubber opened in Los Angeles. It quickly became surrounded by a fog of beautiful, eye-irritating, orange vapor: Smog had been born. The catalytic cracking of petroleum, which began on a large scale at this time, led to the production of a vast array of unsaturated hydrocarbons, and soon the aerosol we now know as smog was not only generated abundantly in industrial Los Angeles but also drifted from Los Angeles inland to the San Gabriel Mountains. It travelled east as far as Riverside and even New Jersey! The aerosol, contained under the inversion layer characteristic of summer and fall days in southern California, could not rise up and be diluted.

In the late 1940s, no one knew the chemical nature of the smoggy aerosol, although it was widely suspected that it had something to do with emissions of petroleum products. The Western Oil and Gas Association, the industrial association of petroleum companies, engaged the services of the southern branch of Stanford Research Institute to determine the chemical nature of smog. They found that smog was caused by sulfur dioxide emissions. Stringent laws were immediately passed in Los Angeles County, putting a lid on SO_2 emissions, and soon Los Angeles had the cleanest air—from the standpoint of SO_2 pollution—of any major city of the United States.

But smog continued to get worse, and at this point Haagen-Smit intervened. His training and experience in microchemistry—that is, the determination of the chemical nature of substances available only in very small quantities—stood him in good stead. He and his constant colleague, Charles E. Bradley,[4] determined that the aerosol was composed of polymerized oxidation products of unsaturated hydrocarbons. They further showed that these unsaturated hydrocarbons were released from gasoline storage tanks, from the gasoline tanks of automobiles, and were also present in the exhaust of automobiles. Further study showed that the formation of smog was even more complicated because it was not due to unsaturated hydrocarbons alone, but to their oxidation by ozone.

Early in the course of these investigations (work done in collaboration with Milton Zaitlin, Herbert Hall, and W. Noble) it was also found that smog injured plants. Sensitive plants such as spinach and alfalfa were used for sometime to determine smog severity at smog-measuring stations throughout Los Angeles County. Haagen-Smit and Charles Bradley also worked out a simple quantitative method for

[4] Charles E. Bradley was the retired head of chemical research for the United States Rubber Company and the first professional chemist ever employed in the rubber industry in the United States.

determining ozone concentration in the air: Put a piece of bent, and therefore stressed, rubber tubing into an air sample and determine how long it takes for the stressed rubber to crack—a simple, elegant, and quick test for ozone concentration in air.

The single, localized smog source of 1943 was quickly controlled by the reduction of leaks from the butadiene plant. In the years after 1943, however, smog in Los Angeles grew ever more intense and pervasive. In 1947 the Los Angeles County Air Pollution Control District was formed by an act of the California legislature to study the problem. It was also provided with the legal tools to enforce measures necessary for improving the situation. Haagen-Smit was instrumental in persuading city, county, and state officials to establish this organization and institute these important measures. By the late 1940s, Haagen-Smit not only knew the nature of smog, he realized the magnitude of the problem of dealing with it and the need for action on a wide front. More research was needed, for example, to find out in detail how the high oxidant levels in Los Angeles air were generated.

From 1950 to 1959, Haagen-Smit took a year's leave of absence from his academic post to lead the research efforts of the Los Angeles County Air Pollution Control District. These further studies confirmed the details of the photochemical cycle by which primary pollutants were transformed into eye irritants and polymeric aerosols. The primary agents in this process were the oxides of nitrogen that originated in all high-temperature combustion in air (the combination of oxygen and nitrogen at high pressure and temperature and the rapid quenching of the reaction). These conclusions were not at all readily accepted by the automobile industry, however, and it was not until 1954 that general agreement as to the chemical nature of smog and the photochemical nature of its genesis was achieved.

Even so, the story of the study of smog is in large part the story of Arie Jan Haagen-Smit single-handedly fighting the resistance of the American automobile industry. The industry gradually gave in, bit by bit. One day, for example, I saw Haagen-Smit chuckling in the hall and asked him what was so funny. He said, "Today I had three vice-presidents from the Ford Motor Company in my office. Last year I would have had to go to Detroit to see them, if I could have seen them at all."

Automobiles, however, were not the only producers of hydrocarbons. The enormous oil-fueled electric power plants in southern California were also major producers of air pollutants, and in 1957 Haagen-Smit took a further leave of absence to study the control of air pollution in the plants of the Southern California Edison Company. Through these investigations he was able to bring about major reductions not only in hydrocarbon emissions but also in the emission of nitrogen oxides. And in 1960, when the state of California established a motor vehicle pollution control board, Haagen-Smit chaired its criteria committee. He also lobbied for, and was instrumental in the formation of, California's Air Resources Board. In 1968 he became its chairman.

In this position, he was responsible for enforcing the Board's regulations concerning maximum allowable pollutants in automobile exhausts. Each car manufacturer was required to certify at the beginning of each model year that its models conformed to California emission requirements. If a company's cars did not conform, it was not permitted to sell cars in California. One year (I think it was in 1969) the Volkswagen Company failed to register its compliance with the Air Resources Board regulations. Haagen-Smit promptly posted a ban on the sale of Volkswagens in the state. He took enormous flak from the entire automobile industry but the ban stood, and within ten days Volkswagen produced its certifi cate of compliance. As Haagen-Smit said at the time, "I'm sorry it wasn't General Motors, but, in any case, that's real power!"

Haagen-Smit had the courage and conviction to give up his more academically respectable studies to attack the urgent social problem of smog. Unlike most scientists, he did not stop at identifying the problem but went on to implement its cure. The polluting effects of the automobile would have remained unchecked but for his influence on legislation at the county, state, and national level.[5] Rigorous of thought, humorous, and persuasive, he was instrumental in establishing the Los Angeles County Air Pollution Control District. His recommendation that California establish a statewide Air Resources Board was promptly adopted by the state legislature, with Haagen-Smit appointed as the Board's chairman. He was successful at every step of his quest for more stringent air pollution control legislation and was directly responsible for the catalytic converters now mandatory on automobiles to remove the last vestiges of unburned hydrocarbons from their exhausts.

Haagen-Smit retired from Caltech in 1971 but retained his position as chairman of California's Air Resources Board until 1973. He continued to work on smog abatement and had the pleasure of attending the dedication of the new Arie Jan Haagen-Smit Laboratories of Air Pollution Research of the Air Resources Board. He was also a member of the President's Task Force on Air Pollution (1969-1970) and a member of the Environmental Protection Agency's National Air Quality Advisory Committee from 1971 to 1976.

Haagen-Smit contributed his creativity and energy to the

[5] Haagen-Smit was widely regarded—internationally as well as nationally—as the authority on smog and air pollution and on methods for diminishing such pollution. So universal was his fame that he was known to all local residents of southern California as "Dr. Haagen-Smog."

problem of smog control in every way he could manage. In a thoughtful mood he once said to me: "I have studied the chemical nature of smog, and I've studied where it comes from. I've studied how to control the sources and the political measures necessary for regulation of emission of pollutants. I've done it on a local basis and I've taken it to the state basis and I've done quite a bit on a national basis. There's only one facet of air pollution control that I think I could have done more for and that's city planning." But this is characteristic Haagen-Smit modesty. So far as smog and its elucidation and control are concerned, Haagen-Smit did it all.

He passed away March 18, 1977.

HONORS AND DISTINCTIONS

Boards And Committees

1943-1946 Chairman, Netherlands-American Society

1945 Chairman, Southern California Section, Society for Experimental Biology and Medicine

1950-1960 Member Advisory Committee, American Cancer Society

1962 Southern California Section, American Chemical Society, held various offices from 1950 on; Chairman, Board of Trustees

1950-1972 Los Angeles County Air Pollution Control District, Senior Consultant

1954 Member, State Committee of Technical Experts on Air Pollution (Beckman Committee)

1955-1960 Member, Environmental Health and Air Sanitation Advisory Committee, State of California

1957-1958 Consultant, Southern California Edison Co.

1960 Member, Los Angeles County Medical Assoc. Committee on Environmental Pollution

1960 Member, Clean Air Committee for Los Angeles area, L. A. Chamber of Commerce

1960-1962 Member, Motor Vehicle Pollution Control Board, State of California

1967-1970 Trustee, Arboretum Foundation of Los Angeles County; President (Honorary Trustee 1971-1977)

1963 Member, Presidential Advisory Panel on Environmental Pollution, U.S. Office of Science and Technology

1964-1973 Member, Advisory Committee for Biology and Medicine, Atomic Energy Commission

1965 Member, Committee on Pollution, Subpanel on Air, National Academy of Sciences

1967 Member, Technical Advisory Panel to the Assembly Committee on Transportation and Commerce, California State Legislature

1967-1968 Chairman, Technical and Scientific Advisory Committee, State of California Air Resources Board

1968-1973 Chairman, State of California Air Resources Board

1968-1971 Member, Environmental Health Sciences Advisory Committee, U.S. Department of Health, Education & Welfare

1969-1972 Member, Governor's Environmental Quality Study Council

1969-1970 Chairman, President Nixon's Task Force on Air Pollution

1970-1971 Member, Advisory Committee on Application of Aerospace Technology, for Mayor of Los Angeles

1971 Member, Sea Grant Advisory Panel, University of Southern California

1971 Member, Environmental Control Seminar Programs in Rotterdam, Warsaw, Prague, and Bucharest, for U.S. Department of Commerce

1971 Member, Conference of Interdisciplinary Communications Program, Smithsonian Institution

1971 Member, Committee for Motor Vehicle Emissions, National Academy of Sciences

1971 Member, Editorial Board, Excerpta Medica (The Netherlands)

1971-1973 Chairman, National Air Quality Criteria Advisory Committee, Environmental Protection Agency

1972 Reviewer, Extramural Research Projects and Grants, Environmental Protection Agency

1973 Consultant, Division of Biomedical and Environmental Research, Atomic Energy Commission

1974-1976 Member, Science Advisory Board, Environmental Protection Agency

Honors And Awards

1947 Knight of the Order of Orange Nassau, The Netherlands

1950 Fritzsche Award, American Chemical Society

1955 Certificate, Pure Air Committee

1957 Special Clean Air Award, Los Angeles County

1958 Frank A. Chambers Award, Air Pollution Control Association

1959 Medal of Merit, Daughters of the American Revolution

1964 Richard C. Tolman Award, Southern California Section, American Chemical Society

1969 Hodgkins Medal, Smithsonian Institution

1969 Fellow, The Franklin Institute

1970 B. Y. Morrison Memorial Lectureship Award, Agricultural Research Service, U.S. Department of Agriculture

1972 Honor Scroll, American Institute of Chemists

1972 Frederick Gardner Cottrell Award, National Academy of Sciences

1972 Monsanto Award for Air Pollution Control, American Chemical Society

1973 National Medal of Science

1974 Rheinland Preis (Germany)

1974 Tyler Ecology Award

1974 Eliot Cresson Gold Medal, The Franklin Institute

Professional Societies

Air Pollution Control Association
American Chemical Society
American Association for the Advancement of Science
Botanical Society of America
Botanical Society of The Netherlands
Dutch Chemical Society
Institute for Food Technology
New York Academy of Sciences
Royal Academy of Science, The Netherlands
Sigma Xi
Society for Experimental Biology and Medicine
Society of Plant Physiologists
Society for the Study of Development and Growth
Swiss Chemical Society
Alpha Chi Sigma
National Academy of Sciences

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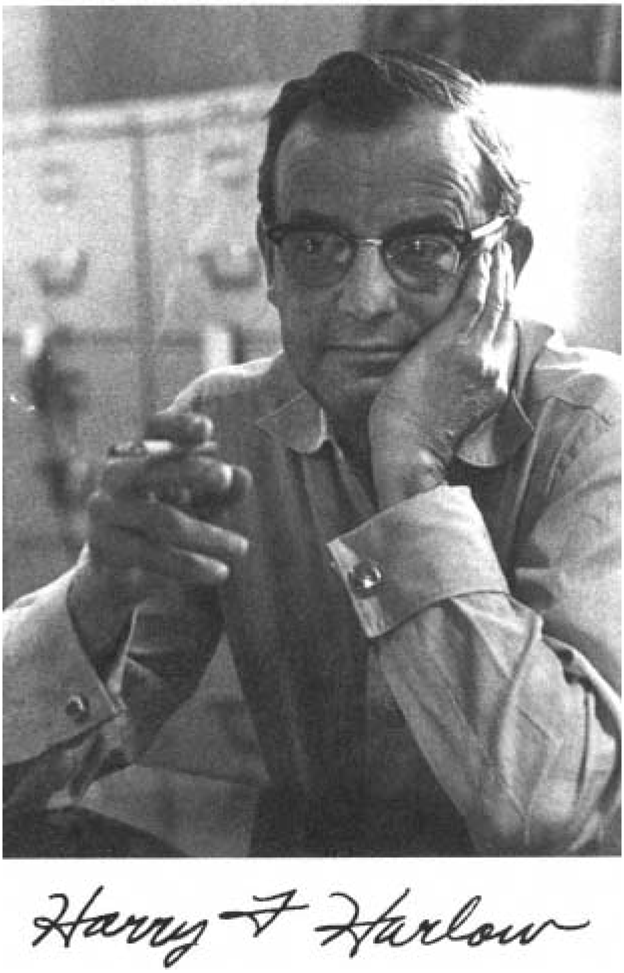
Harry F Harlow

Harry Frederick Harlow

October 31, 1905-December 6, 1981

By Joseph B. Sidowski and Donald B. Lindsley

Harry Harlow was born Harry F. Israel in Fairfield, Iowa, the third of four sons born to Lon H. and Noble (Rock) Israel. For reasons unknown, he changed his name legally to Harlow while in college. After forty-four years of association with the University of Wisconsin (1930-1974), he became professor emeritus and retired to Tucson, Arizona, where he served as honorary research professor of the University of Arizona. In his later years, he suffered from Parkinsonism. He died of a brain tumor in 1981.

ACADEMIC YEARS

Harry Harlow, as he himself described it, was a shy, retiring, and callow youth when he began his college studies at Reed College in Portland, Oregon, in 1923. After one year he decided to follow his brother to Stanford University, where he would receive his B.A. degree in 1927, majoring in psychology. His original intent had been to major in English, but an unfavorable grade in that subject and an exciting introductory course in psychology changed his mind. His poetic nature and an ability to use the English language in a humorous manner remained, later contributing greatly to his success both as a teacher and a professional lecturer.

While still an undergraduate, Harlow supported himself working as an assistant to the experimental psychologist Walter R. Miles, who was elected to the National Academy of Sciences in 1933. As a graduate student at Stanford, Harlow came under the tutelage of Calvin P. Stone, who was elected to the Academy in 1943. As a graduate student, Harry held a teaching assistantship under Paul R. Darnworth in social psychology and research assistantships under Stone in behavioral studies on rats. His doctoral dissertation dealt with the social facilitation of eating behavior in rats, combining elements of his ongoing experiments as an assistant. Much later, Harlow said that he learned scientific methodology and techniques from Stone, but he always considered Miles his moral and ethical mentor.

He admired Lewis W. Terman, then head of the department of psychology, and learned about theory in psychology from him. Terman had been elected to the Academy in 1928. Toward the end of Harry's second graduate year, Terman wrote to Harlow's mother of his great progress in psychology and his preparation for academic teaching and research. However, later when Harry was seeking an academic position, Stone, Terman, and Miles all advised him to consider a junior college position because of a speech defect, which they thought interfered with his ability to articulate clearly and sometimes brought forth smiles when he said "wat" for rat!

Despite this advice, he accepted a position as an assistant professor of psychology at the University of Wisconsin in 1930, where he regularly taught the large introductory class in psychology. With determined application, his diction and enunciation steadily improved, and he became one of the most effective and popular lecturers on campus. It was probably with these student audiences that he developed his unhurried, clipped manner of speech that—along with his creative intellect and great wit—ultimately made him one of the most entertaining, effective, and sought after speakers in all of psychology.

Hired as a comparative animal psychologist, Harlow arrived at the University of Wisconsin in 1930 to learn that there was no animal laboratory. However, he soon found a cramped cubicle in which to house his rats, which happened to be just below the office of the Dean of Men who didn't appreciate the odors wafting upward.

As a result, Harry was displaced from that location and given a small space in the University Medical School. There he began studies of the social facilitation of feeding responses in monkeys, an extension of his doctoral research with rats. But that space, too, proved vulnerable and temporary, and his first steps into a major career dedicated to the study of nonhuman primate behavior began at a bridge party, when the wife of the chairman of the psychology department suggested that he study primates at the local Vilas Park Zoo. The Zoo afforded an opportunity to work with a variety of primates, including an orangutan, baboons, and monkeys, experiences that were to prove invaluable and would lead to an unexpected turn in his career.

PRIMATE LABORATORIES AND RESEARCH

Harlow's first primate research facility consisted mainly of a few tables, a test tray, and test objects at the Vilas Park Zoo. In 1932 the University of Wisconsin made available to him a very small, two-story structure that had previously been the Forest Products Laboratory. It was badly in need of renovation. With his own meager funds and the aid of Walter Grether, Paul Settlage and other graduate students this was accomplished. The result was a usable research facility and the first real primate laboratory in Wisconsin's Department of Psychology.

Acquiring a small colony of monkeys, Harlow and his graduate students enthusiastically began developing new and unique ways to study primate behavior, both qualitatively and quantitatively. Using the oddity principle and matching-from-sample procedures they were able to study perceptual discrimination involving figures and patterns on visual displays or objects that differed in color, size, shape, or texture. By introducing time delays between stimulus presentation and opportunity to respond (method of delayed response), they could study both learning and memory decay. Combining different tasks in so-called test batteries they could explore and identify the nature and extent of "animal intelligence" in various species as well as in humans. In order to conduct these experiments in a uniform way they designed and built a standard piece of equipment, known as the Wisconsin General Test Apparatus (WGTA). This device was adopted and used by many investigators over the years, even until recent times.

One of the most significant discoveries Harlow and his associates made in their first primate laboratory dealt with the formation of *learning sets*, that is, the process by which animals "learn to learn." Their procedure was to present pairs of objects or patterns that differed in features such as size, color, and shape over a series of trials. The objects changed every few trials, and the animal gradually learned to abstract particular features that differentiated the correct response object from others. In this way, discrimination cues became generalized and a *learning set* was established. Harlow and his students, as well as others, exploited this technique in the study of brain lesions and other experimental variables.

The origin and concept of the *learning set* idea was not sudden. From 1939 to 1940, during a sabbatical year, Harlow held a Carnegie fellowship at Columbia University with famed anthropologist Franz Boas. While at Columbia he attended a seminar by the German neurologist Kurt Goldstein and became familiar with his theories concerning abstract and concrete intelligence and learning, which relied heavily upon performance on block-sorting tests such as the Weigl or Vigotsky tests. In these tests small wooden blocks varying in size, color, and shape must be sorted and grouped according to one or more of such categorical features and the principle of a category identified. According to Goldstein, only humans are capable of abstract thought. Harlow tentatively disagreed. Upon returning to Wisconsin he pursued research that eventually demonstrated—contrary to Goldstein's view—that monkeys could also solve Weigl and Vigotsky type problems, suggesting certain levels of abstract thought and reasoning. These results, together with those from his earlier studies of oddity and matching-to-sample discriminations caused Harlow to focus on the question of methodology.

Limited by cost, upkeep, and availability of monkeys, Harlow was forced to ignore the usual experimental procedures of the time; that is, use of naive and different animals for each condition or problem, as was the practice with cheap and plentiful rodents. He used the same monkeys for the study of a variety of problems. If separate groups of monkeys had been used to learn single, simple discriminations, he might not have discovered the concept of *learning set*. He further realized that subjecting monkeys to series of similar but related problems paralleled the situations in which children learn.

At a time when Thorndikian trial-and-error learning was at variance with the "Ah ha!" solutions attributed by Gestaltists to sudden insight, Harlow presented results on multiple-problem solution to explain how animals learn-to-learn a problem-by-problem exposition of the bridges between trial-and-error learning and insight. These results posed additional difficulties for the conditioning theories of Clark Hull and Kenneth Spence, influential learning theorists at that time. Sometimes bitter arguments ensued, but Harlow's results and interpretations could not be denied. His *learning set* results were enthusiastically received when presented in his Presidential Address before the Midwestern Psychological Association in 1948. The subsequent wide acceptance of these results undoubtedly enhanced his reputation as a creative scientist and with it his confidence in his general approach to scientific investigation. Ahead of their time, these studies oriented the methods and thinking of modern cognitive psychologists toward natural as opposed to contrived information processing.

Another notable accomplishment involved investigations of newly conceived and identified *curiosity* and *manipulation drives*, in cooperation with Robert A. Butler, Donald R. Meyer, and Harry's wife, Margaret Kuenne Harlow, a child psychologist. At a time when drives were considered to be wholly or partly physiological, Harlow and his associates established the fact that the curiosity and manipulation drives were intrinsic parts of the rhesus monkey's motivational structure. Food, water, and sex were not found sufficient or necessary to initiate behaviors resulting from curiosity and manipulation drives. Monkeys were just naturally curious and would work hard, if necessary, to satisfy their curiosity. They would, for instance, manipulate mechanical puzzles incessantly without the rewards deemed necessary by behavioral theorists of the day. Furthermore, Harlow's monkeys learned complicated tasks without being deprived of basic necessities such as food and water.

Along with the foregoing studies of a strictly behavioral and psychological nature, which had such an important bear ing on theoretical issues with regard to motivation, drives, and learning, Harlow and his colleagues engaged in a program of neurophysiological and behavioral studies in an effort to determine the role of the central nervous system, and especially the cerebral cortex, in conditioning, visual discrimination, learning, and memory. The need for more refined behavioral tests in connection with these brain lesion-behavioral studies led to the Wisconsin General Test Apparatus (WGTA) and to a great variety of test batteries and procedures.

In pioneering investigations with Stagner (1933) and Settlage (1939), as well as in one of his own studies (1940), Harlow sought to determine whether a classical Pavlovian conditioned response could be established in the cat if, during the normal training procedure, the paw-lifting response to the unconditioned stimulus (shock) was eliminated or modified by curare paralysis. Testing for the response to the conditioned stimulus (tone or light flash) was done after the curare paralysis had worn off. Apparently the assumption was that everything, including the motor discharge blocked by the curare at the neuromuscular junction, would be the same, except for the absence of the paw-lifting response to shock. After an appropriate period of training, and when the muscle was free of paralysis, they found that no conditioned response could be elicited. Although this appeared to be a landmark discovery, there were obvious flaws in the hypothesis, for proprioceptive feedback was also eliminated by the lack of movement caused by the curare. Furthermore, the result was subsequently shown by others to be inconclusive when it was found that curare had a depressing effect on the central nervous system, as well as a paralyzing action at the neuromuscular junction. Harlow then abandoned this type of research, but many years later he considered that decision to be a mistake. In hindsight he felt that he had been on the verge of an important discovery that was not unearthed until years later by other investigators.

From about 1940 on, Harlow, his students, and associates made repeated attempts to determine the effects of brain lesions and ablations on the ability of monkeys to make sensory discriminations and perform various tasks on tests developed for use in the WGTA. Many of these studies resulted in important contributions, but very little of major significance evolved, compared with the earlier and later areas of investigation with which Harlow was associated. One set of studies conducted by Harlow and Dagnon (1943), Spaet (1943), and Campbell (1945) may be mentioned for its pioneering importance in the clarification of an issue with regard to the function of the prefrontal cortex in monkeys. Carlyle Jacobsen, working in the laboratory of physiologist John F. Fulton at Yale in the 1930s, had studied the delayed response performance of monkeys following prefrontal cortex ablations and found that the monkeys could not seem to determine which foodwells had been baited prior to the time-delay introduced in the delayed response test. Jacobsen reported that the prefrontal cortex lesions had caused a deficit in immediate and short-term memory.

Harlow and his associates had found variability in the performance of their lesioned monkeys, but there was clear evidence that some monkeys could manage the time-delays and other discriminations that would not have been possible with severe memory deficits. Instead, they attributed the variability and the sometimes poor performance to an inability to attend to the task and avoid distractions. These results, however, were antedated by the publications of Malmo (1942) and Finan (1942), who used equipment and procedures like Jacobsen's except that the experimental chamber was in complete darkness to insure that the monkeys' attention was focused only upon the stimulus panels, thus avoiding distractions. These findings were later confirmed by French and Harlow (1962). Thus, Jacobsen's putative memory loss results could now be interpreted as due to distraction and inattention rather than an inability to form, store, and retrieve memories after prefrontal lobe ablations. Such results, whether interpreted as attention or memory deficits, had important implications for the performance of human frontal lobotomies, initiated in 1936 by the Portuguese neurosurgeon Antonio Egas Moniz and continued through the 1940s and into the 1950s before being generally abandoned, despite some reported improvement in depressive and other psychopathological conditions. Earlier recognition of the disadvantages of such operations as revealed by animal studies like Harlow's might have forestalled the vast number of lobotomies performed.

In 1932 Harlow moved into a two-story building that was to be his laboratory for the next twenty years. This building had less than the desirable amount of space in which to fit a small colony of monkeys, graduate students, postdoctoral visitors, laboratory equipment, and facilities for experimentation. It also lacked the necessary office and desk space for the analysis and storage of research data. Furthermore, it was in the early stages of the Depression and financial support was in short supply everywhere. There were, of course, no federal granting agencies at that time to support research and training fellowships for graduate students, as there would be later in the 1950s and beyond. These, however, were problems faced by most college and university professors lucky enough to have a job.

It is said, "Where there is a will, there is a way!" Harry had a will, and he found a way. He was highly motivated and had recently found a goal that would become a lifetime endeavor: focus on the rhesus monkey (*Macaca mulata*) as an experimental model for the study of the neural and behavioral aspects underlying human psychology. He soon found that not the least of his problems was the upkeep and survival of his monkeys. Over the next twenty years he developed the experience and knowledge necessary to sustain primates over long periods of time within animal enclosures, though they enjoyed only a few summer months of the warm weather typical of their natural habitat. It was also in this laboratory that Harlow supervised his first Ph.D. student, Abraham Maslow, who later developed the self-actualization theory of motivation and was credited with being one of the founders of the humanistic psychology movement.

In 1953, the primate laboratory operations were moved from their initial location to a renovated cheese factory several city blocks from the campus. The motivational, learning, and neurophysiological-behavioral research was continued and expanded, resulting in a need for more monkeys. Fortunately, the space was now adequate. Because of import problems, disease, and the cost of the monkeys, the decision was made to start a breeding colony of rhesus monkeys. There was virtually no information available on the care and rearing of laboratory-born monkeys. Methods were devised through trial, error, and observation to enhance the probability that the newborns would survive.

Initially, forty infant rhesus monkeys were separated from their mothers and raised in separate cages. The result was disease-free animals that manifested bizarre and psychopathological behaviors. These abnormal behavior syndromes were attributed to the effects of early isolation and led to some of Harry Harlow's most fascinating and best-known research. The breeding, rearing, and nursery procedures proved successful overall, and a subsequent published report with A. J. Blomquist served as a guide for breeders in other animal installations, including zoos. Harlow's infant pri mate care methods were eventually adopted in many places around the world.

The availability of laboratory-born infants led to the study of the ontogeny of learning and the development of agesensitive learning tests, some of which showed that learning-set formations did not develop until approximately twelve to eighteen months of age. They provided interesting data for comparison with the age-level stages of intelligence and mental growth established by Jean Piaget, the famous Swiss child psychologist. But the infant rhesus macaques were to produce even better known data, specifically in the areas of affection and love.

Harlow's research on affectional systems evolved primarily from a bizarre result of infant isolation: the inability to reproduce upon reaching maturity. This, of course, influenced the supply of research animals. To remedy this situation, Harlow thought of a way to provide "mothering" of a sort to the isolated infants by developing surrogate mothers. He had earlier noted the strong attachment of infant monkeys to their diaper cloths. This led him to the idea of a cloth-covered wire framework resembling a monkey mother. The concept of a surrogate mother was not new; it was Harlow's genius in creating simple experimental situations in which to use the surrogate that was novel and important. With the aid of graduate student Robert Zimmerman, surrogates were built to replace the biological mothers in attempts to "normalize" the behavior of the isolated infants. Some of the surrogates were made of bare wire; others were covered with terrycloth. Other maternal characteristics were added, such as protruding rubber nipples for the supply of milk, internal temperature controls for warming or cooling, and mechanical arrangements for providing gentle rocking motion. Subsequent studies showed that an infant's attachment to its surrogate mother was due as much to "contact comfort" as it was to nourishment provided by feeding. Also, the warmth and rocking were found to be important factors.

Very important to Harlow was the fact that he had now found a way to raise disease-free monkey infants in isolation. Surrogate mothers now provided warmth, comfort, and sustenance in an environment that could be controlled and modified as required by experimental research programs. The tempo and scope of the infant monkey research now increased and many studies were undertaken, the results of which often interested psychoanalysts and challenged psychoanalytic theory as well as traditional learning theory.

When social development of surrogate-mother-raised and biological-mother-raised monkey infants was compared, it was found that natural genetic mothers were significantly better at socializing the young. The importance of peer relationships was studied by raising infants together and away from adult animals, and it was found that the presence of peers and play opportunities was important to the process of social development. Some of the data indicated that the peer-to-peer interactions were more important than those between mother and infant. Harlow reported that one of the most important relationships determining normal sexual behavior as adults was the peer play during infancy and childhood of these monkeys.

Laboratory research extended into the abnormal as well as the normal behaviors. The bizarre behaviors resulting from isolation were used as a basis for studying the long-term effects of isolation *per se*. Animals separated from their mothers at birth and isolated for periods of six months or longer showed deficits in social, sexual, and other behaviors. The longer the isolation, the worse the deficit. Impregnated, sexually mature female isolates showed few of the normal mother responses expected of rhesus females. In some cases these motherless-mothers grossly abused their newborns, in dicating the importance of early socialization in the learning of proper care taking and mothering behaviors.

"Love created, love destroyed, and love regained" guided the affectional-systems research Harry pursued with his wife, Margaret Kuenne Harlow. Love was created by parental-infant, peer-peer, and surrogate-infant attachments. Isolation and separation led to its destruction. Systematic rehabilitation with a younger monkey (a peer, social-modeling therapist) resulted in love regained.

The reactions of isolate-raised infants separated from their mothers were akin to those of human infants suffering from anaclitic depression as described by British psychiatrist J. A. Bowlby. When peer-reared monkeys were separated for several days similar kinds of depressed behaviors were noted by Harlow and S. Suomi, and the pattern persisted.

Love was regained by rehabilitation, mainly with younger monkeys. A series of studies with infants isolated from birth for various periods of time indicated that placement with normal, same-age mates or with mature females who experienced normal mothering was essentially unsuccessful in socializing the "depressed" monkeys. The aggressive and dominant behaviors of these animals were not changed. However, placement of "depressed" monkeys with younger normal monkeys immediately upon release from isolation eventually led to play and socialization. This therapeutic technique, developed with Suomi, was later used with some success by others in rehabilitating institutionalized human children diagnosed as depressives.

Harry and Margaret Harlow also collaborated in research on the activities of monkey nuclear families living in adjacent enclosures. The setting allowed for the study of infant interactions, fathering, and other relationships. Harlow pursued the research on monkey nuclear families and depression until his retirement from Wisconsin. He believed, however, that his most significant contributions came out of his surrogate studies on love, isolation effects, and psychopathology. Harlow often said that when you work with monkeys, you think of human problems, and he believed that human data generalized to monkeys very nicely, if not vice versa.

From a general purview of his many scientific and professional publications, it is difficult to pinpoint a central theme. His main goal, it seems, was to study a single species, the rhesus monkey, to learn all he could about its behavior and cognitive processes, and to relate the results to humans. The first decade of his tenure at the University of Wisconsin was dedicated to finding suitable laboratory research facilities. Then he strove to find the best empirical methods for working with monkeys and to develop unique tests for assessing their sensory and perceptual abilities and the motivational circumstances under which they worked best at solving graded levels of problems and tasks. This led to the development of elaborate and creative test batteries and the WGTA, all of which benefitted and stimulated his many students and others throughout the world. He turned briefly to the cat to investigate further the nature of the conditioned response. During the next three decades Harry and his students and colleagues used monkeys and the WGTA tests to try to locate in each of the principal regions of the cerebral cortex the extent to which various functions were subserved, eliminated, or modified under the influence of anaesthesia, radiation, and ablation.

Understanding the neural basis of behavior never seemed to interest him as much as understanding behavior itself. He concentrated on behavior studies with monkeys throughout the last three decades of his life, opening up new vistas with regard to the cognitive aspects of behavior and the social and affective consequences of manipulation of the environment on early development. Harry Harlow was a deductive, qual itative empiricist and phenomenologist, whose greatest discoveries and contributions resulted from planned serendipity. Serendipity even entered into his poetry, which he created quickly and freely and often injected into his publications and talks.

OTHER SCIENTIFIC AND PROFESSIONAL ACTIVITIES

By his own admission, Harlow was more of a nativist, who believed in the inheritance of characteristics to a greater extent than many of his contemporaries in psychology. Yet this personal inclination was not strongly reflected in his research, which in its cognitive and social aspects emphasized environmental influences. He foresaw the importance of biochemistry in studies of behavior, and in 1958 he coedited a volume on the *Biological and Biochemical Bases of Behavior* with neurophysiologist Clinton N. Woolsey, also of the University of Wisconsin and a member of the National Academy of Sciences. The book resulted from a symposium they had planned jointly and was a pioneering example of interdisciplinary research. A year later he collaborated with N. A. Waisman, a pediatrician interested in the genetic basis of phenylketonuria in monkeys and humans.

Although not directly involved in the space program, the Wisconsin Laboratory supplied one of the first monkeys sent into space. In 1954 Harry cooperated with aerospace pioneer D. C. Simons on a series of stratospheric plastic balloon flights to study the effects on monkeys of exposure to radiation above 90,000 feet. (At the time, low energy, heavy nuclear particles of primary cosmic radiation could not be reproduced with available accelerators.) At about the same time, he was involved in investigating the behavioral effects of cortical implantations of radioactive cobalt.

During a two-year leave from the University from 1950 to 1952, Harlow served with the Department of the Army in the Pentagon as chief of the Human Resources Branch. In that position, he was responsible for proposing the establishment of a Human Resources Research Office for the conduct of psychological research. The recommendation was implemented in 1951 and the office established on the campus of The George Washington University, with Meredith Crawford as its director. With Phillip Sapir of the National Institute of Mental Health, he collaborated in the cofounding of the NIMH Small Grants Program.

From 1951 to 1963, Harlow served as editor of *the Journal of Comparative and Physiological Psychology*, using that position to advance primatology. The proportion of publications dedicated to primate behavior increased noticeably over the twelve years of his editorship. He also encouraged the publication of articles on the developmental aspects of psychology and behavior, but the number of manuscripts in those areas proved disappointing.

In 1964, one of the seven national Regional Primate Research Centers was established adjacent to the University of Wisconsin Primate Laboratory. Harlow served as its director until 1971.

Harry F. Harlow was elected to the National Academy of Sciences in 1951 and to the American Academy of Arts and Sciences in 1961. At the 52nd meeting of the Society of Experimental Psychologists in 1956, he was awarded the Warren Medal for "a series of brilliantly conceived experiments on the behavior of monkeys, including studies of motivation, learning, and problem solving." From 1958 to 1959, Harlow served as president of the American Psychological Association; in 1960, he received its Distinguished Scientific Contribution Award for "curiosity and imagination which opened up new areas of research in animal behavior and enhanced the position of comparative psychology."

President Lyndon B. Johnson presented him with the Na tional Medal of Science in 1967, and in 1973 he received the Gold Medal Award of the American Psychological Association. Harlow accepted the Kittay Scientific Foundation Award in 1975 for his use of monkey models to study psychopathological behaviors. The Primate Laboratory at the University of Wisconsin was dedicated and named in his honor in 1984.

Harry Frederick Harlow was an unassuming man of many talents. He was a poet and gifted writer, an excellent bridge player, and a pretty good locally competitive tennis player. He was generous in sharing time and ideas with students who wished to set up primate laboratories elsewhere. His long walks with professional colleagues and graduate students were legendary, as were his many professional talks.

Harlow married Clara Mears in 1932. Two sons, Robert and Richard, were born of this union. In 1946 the marriage was dissolved and each party later remarried. In 1948, Harry married Margaret Kuenne, a child psychologist of note, with whom he collaborated on numerous research, publication, and editing activities. Two children, Pamela Ann and Jonathon, were born of this marriage. Margaret died of cancer in 1971. Shortly after her death, Harry and Clara, his first wife (then a widow) remarried. Upon his retirement from the University of Wisconsin in 1974, Harry and Clara moved to Tucson, Arizona, where Harry held an honorary appointment at the University of Arizona. He and Clara collaborated on several publications, the most notable being a book entitled, *The Human Model: Primate Perspective*, published in 1979. Harry died in 1981.

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Charles Heidelberger

Charles Heidelberger

December 23, 1920-January 18, 1983

Elizabeth C. Miller and James A. Miller

Charles Heidelberger was a scientist with broad talents. Trained as an organic chemist, he later became a skilled biochemist and cell culturist. From his many years of research on cancer chemotherapeutic agents, he also developed an impressive knowledge of human cancer and its treatment. He was a prolific reader, an original thinker, a synthesizer of ideas, an avid explorer of new concepts, and a lucid writer. Using these talents and his fine intellect, Charles Heidelberger made his mark in science by seminal and extensive contributions to three areas of cancer research. He pioneered in the use of ^{3}H- and ^{14}C-labeled carcinogenic polycyclic hydrocarbons in the study of their metabolism and their interactions with target tissues. He was an early investigator of the development of systems for the malignant transformation by chemicals of mammalian cells in culture, and—with his colleagues—he developed one of the most widely used systems for the transformation of mouse fibroblasts. His most important accomplishment, however, was the design, synthesis, preclinical testing, and analysis of the mechanisms of action of 5-fluorouracil (5-FU) and related compounds for the chemotherapy of cancer.

EARLY YEARS

This remarkable scientist was born on December 23, 1920, the only child of Michael and Nina (née Tachau) Heidelberger. Known as Charlie to his many friends, Heidelberger was most fortunate to be brought up in a warm and loving family that included the arts and sciences among its many interests. In addition to his parents, his immediate family in New York City included his mother's mother and five of his mother's sisters. Charlie's grandmother was much beloved by the whole family. She and her daughters, Charlie's aunts, maintained close relations with the Heidelbergers. Both Nina and Michael Heidelberger had a talent for and interest in music, and they made their home a center for its enjoyment. At the time of Charlie's birth, Michael Heidelberger was already established at the Rockefeller Institute for Medical Research as a promising young organic chemist. Thus, from his earliest years, Charlie came to know scientists, both from the United States and Europe, and to hear discussions of their work. In an account written during his last year of high school Charlie listed Drs. O. Avery, R. Loeb, and W. Osterhout—all of the Rockefeller Institute —among his friends. In addition, as a child, Charlie accompanied his parents on several trips to Europe, through which he gained an early appreciation of the international nature of science and of culture.

Except for summer vacations, Charlie lived in New York City from his birth until he graduated from high school. He attended the Birch-Wathen School, a private school at 94th Street. According to Charlie's account, he passed his early years in a middle- to upper-class school that emphasized learning the fundamentals of science, history, and language. His extracurricular activities in high school included music, drama, and journalism. At about the age of six, Charlie was given a quarter-size violin and a few violin lessons by Toscha Seidel, an eminent musician and family friend, who later presented him with his first full-size violin.

From the age of nine, Charlie spent many of his summers at a boys' camp on Cape Cod, first as a camper and later as a junior counselor. At camp he developed a fondness for and great competence in sailing, which he was to enjoy as an avocation in college, during his twenty-eight years in Madison, Wisconsin, and after moving to Los Angeles.

In 1937 Heidelberger was admitted to Harvard College, where he majored in chemistry. On completing the B. S. degree in 1942, he began his graduate work at Harvard, earning M. S. and Ph.D. degrees in organic chemistry in 1944 and 1946, respectively. His Ph.D. advisor was the eminent organic chemist Louis Fieser, who was then carrying out research on several war-related projects. Accordingly, the second part of Heidelberger's thesis, "The Synthesis and Antimalarial Activity of Some Naphthoquinones," came out of the war effort of Fieser's group. The results of his thesis were published, together with those of his colleagues, in a series of multiauthored papers in *the Journal of the American Chemical Society*. The summer following completion of his Ph.D. degree, Heidelberger was appointed an instructor in chemistry at Harvard, and he gave the summer lectures in organic chemistry while Fieser was on sabbatical leave. Although Fieser had set aside his research on the carcinogenic polycyclic aromatic hydrocarbons during the war years, the laboratory at Harvard introduced Heidelberger to these carcinogens, which became central to his later research. His graduate work also introduced him to chemotherapeutics, his second principal area of research.

For postdoctoral work, Heidelberger moved to the Donner Laboratory of the University of California, Berkeley, where he joined Melvin Calvin and his associates in the study of carbon-14 as a tool for the elucidation of metabolic reactions. During this two-year period, Heidelberger synthesized the first carbon-14-labeled carcinogen, dibenzanthracene-9,10-carbon-14 (now known as [7,12-^{14} C]dibenz (a,h)anthracene) and carried out initial studies on its metabolism in the mouse. At the same time, working with S. Lepkovsky, he synthesized ^{14}C-labeled tryptophan and indole-3-acetic acid for analysis of tryptophan metabolism. This period also saw Heidelberger's preparation, with M. Calvin, J. C. Reid, B. M. Tolbert, and P. F. Yankwich, of the textbook *Isotopic Carbon*. This book, published in 1949, was the standard textbook for students using carbon 14 in metabolic studies for more than a decade.

RESEARCH CAREER

Heidelberger's studies on [^{14}C]dibenz(a,h)anthracene caught the attention of Harold P. Rusch, director of the then relatively new McArdle Laboratory for Cancer Research at the University of Wisconsin. While attending a meeting on the West Coast, Rusch visited Heidelberger at the Donner Laboratory and persuaded him to accept a position as assistant professor of oncology at the McArdle Laboratory. In 1948, Heidelberger and his wife Judith moved to Madison, marking the beginning of his productive twenty-eight years at McArdle.

Heidelberger was brought to the McArdle Laboratory to establish facilities for the use and quantitation of carbon-14 for metabolic studies, to provide expertise in the synthesis of labeled compounds (at a time when they were not commercially available), and to pursue the problem of cancer according to his own ideas. He carried out each of these activities with vigor. Heidelberger soon set up a centralized departmental facility for the quantitation of carbon-14 (and later for tritium and P-32). He kept the facility operating with state-of-the-art technique for nearly thirty years. With his expertise in the use of carbon-14, he collaborated on projects with most of the members of the McArdle staff during his first decade there.

Together with Van R. Potter, Heidelberger initiated his research at the University of Wisconsin with a study to test A. G. Ogsten's theoretical deduction "that the asymmetric occurrence of isotope in a product cannot be taken as conclusive evidence against its arising from a symmetrical precursor."[1] Heidelberger and Potter's study completely confirmed Ogston's theory that an asymmetric enzyme can distinguish between identical groups of a symmetrical compound, demonstrating the asymmetrical synthesis of citric acid labelled with ^{14}C. Potter's interest in exploring a possible metabolic pathway from citric acid cycle intermediates to pyrimidines using orotic acid and Heidelberger's expertise as an organic chemist made them well-suited for collaborative work. They accomplished the synthesis of [^{14}C]orotic acid with Potter's student R. Hurlburt in 1950. Heidelberger's later studies of nucleic acid pyrimidines were built on this experience.

CARCINOGENIC POLYCYCLIC AROMATIC HYDROCARBONS

Heidelberger's synthesis of [^{14}C]dibenz(a,h)anthracene gave him the opportunity to examine the metabolism of this hydrocarbon in much greater detail than had been possible with the spectroscopic methods of earlier workers, and he identified several degradation products. In the late 1940s and early 1950s, when there was great interest in protein-bound carcinogens in target tissues, Heidelberger and his students used labeled hydrocarbons to determine their covalent binding to mouse-skin protein and, especially, to quan

[1] A. G. Ogston, "Interpretation of experiments on metabolic processes using isotopic tracer elements," *Nature* (London), 162(1948):963.

titate the relative levels of binding of several hydrocarbons in relation to their carcinogenic activities. Furthermore, they studied in depth the specificity of binding of the hydrocarbons to various soluble mouse-skin proteins as a function of their carcinogenic activities.

After K. E. Wilzbach (Argonne National Laboratory) reported his general method for the tritiation of organic compounds,[2] Heidelberger prepared tritiated polycyclic aromatic hydrocarbons. The much higher specific activities of the tritiated hydrocarbons facilitated in vivo approaches to macromolecular binding of the hydrocarbons. With G. R. Davenport, Heidelberger was the first to report the covalent binding of a carcinogenic polycyclic hydrocarbon to mouse-skin DNA and RNA. But because of technical problems related to the determination of tritium in cesium chloride solutions in the Heidelberger laboratory, the first definitive report on the covalent binding of polycyclic aromatic hydrocarbons to DNA of target tissues was that of P. D. Lawley and P. Brookes (Chester Beatty Research Institute, London). Using tritiated dibenz(a,h)anthracene, Heidelberger and his colleagues later made one of the first observations of the microsomal metabolism of a polycyclic aromatic hydrocarbon to an epoxide.

The studies on the polycyclic aromatic hydrocarbons were later melded with Heidelberger's work on oncogenic transformation in cell culture. In these investigations, Heidelberger and his colleagues studied the possible relationship between the formation of K-region epoxides of the hydrocarbons and their mutagenic and transforming activities. As this work was being published, the complexity of the metabolic activation of the polycyclic aromatic hydrocarbons and

[2] K. E. Wilzbach, "Tritium-labeling by exposure of organic compounds to tritium gas," *J. Amer. Chem. Soc.*, 79(1957):1013.

the involvement of other sites on the molecules were becoming evident from the reports of P. Sims, P. Grover, and their colleagues at the Chester Beatty Research Institute.[3] Heidelberger and his colleagues continued to probe this area, but other research interests took the lead.

TRANSFORMATION OF CELLS IN CULTURE

As Heidelberger carried out his early studies on carcinogen metabolism in relation to carcino-genesis, he was impressed with the limitations imposed by whole-animal systems on the elucidation of the carcinogenic process. He began, accordingly, to search for other systems. Ilse Lasnitzki had recently shown that organ cultures of mouse prostate glands treated with the carcinogen 3-methylcholanthrene developed an atypical morphology somewhat resembling that observed in tumors. In 1962 Heidelberger took a sevenmonth sabbatical to work with Lasnitzki at the Strangeways Laboratory in Cambridge, England, to learn the techniques required for the development of an organ culture system and to develop a background in the cellular aspects of biology. On returning to the McArdle Laboratory, Heidelberger treated organ cultures of mouse prostate with polycyclic aromatic hydrocarbons, looking for neoplastic properties in the cultures. This laborious work, carried out on a rather large scale, yielded morphologically observable cytopathology but no tumors on transplantation of the cultured cells into isologous mice. In studies with P. T. Iype, however, the hydrocarbon-treated cultures eventually yielded permanent lines of cells that gave rise to transplantable tumors.

This success encouraged Heidelberger and his colleagues to culture C3H mouse-prostate cells for the selection of non

[3] D. H. Phillips and P. Sims, "Polycyclic aromatic hydrocarbon metabolites: their reactions with nucleic acids," in *Chemical Carcinogens and DNA*, P. L. Grover, ed., vol. 2 (Boca Raton, Florida: CRC Press, 1979), pp. 29-57.

malignant cell lines that could be treated with carcinogens in a controlled manner. Such cell lines, which were aneuploid, were obtained, but ceased to grow on reaching confluency. Nor did they produce tumors on inoculation into irradiated isologous mice. But treatment of the rapidly growing cells with 3-methylcholanthrene caused some of them to continue growing after reaching confluency that produced fibrosarcomas on injection into irradiated mice of the same strain. Although malignant transformation of cultured rodent cells by chemicals was achieved somewhat earlier by other investigators, Heidelberger and his colleagues were the first to obtain a system dependent on an established line of cells. Later, Heidelberger-with C. Reznikoff and J. Bertram-established the C3H/10T1/2 cell-line that became a standard tool for studies of mammalian cell transformation and mutagenicity. Heidelberger and his associates showed that there was a general quantitative relationship between the in vivo carcinogenic activities of polycyclic aromatic hydrocarbons and their abilities to cause malignant transformation of these cultured cells. As noted above, they also explored the reactivity of the hydrocarbons with cellular macromolecules in relation to malignant transformation and mutagenesis in culture.

Heidelberger and his colleagues attacked other, more biological, problems with regard to the nature of malignant transformation. These included early explorations of possible retroviral involvement in transformation by chemicals and of stochastic aspects of transformation. They showed that carcinogenic chemicals induced alterations in cells that caused them to become malignant, as opposed to a situation in which the carcinogen facilitated the selection of preexisting malignant cells. They further showed that (as others had demonstrated earlier for malignant transformation in whole animals) each cell line transformed in culture had unique antigenic properties that did not cross-react with those of other independently transformed cells.

CANCER CHEMOTHERAPY

Heidelberger's intellect and energies were such that, from his earliest days at the McArdle Laboratory, he routinely carried out two quite separate research programs in parallel. Starting in the early 1950s, he turned his interest in the biosynthesis of nucleic acids in normal and tumor tissues and—from his graduate student days—in chemotherapy toward a search for pyrimidines that would be therapeutic for cancer. Following a 1954 report by R. J. Rutman, A. Cantarow, and K. E. Paschkis (Jefferson Medical College) on the greater extent of incorporation of uracil into rat liver tumor DNA than into normal liver DNA,[4] Heidelberger made similar observations on a variety of tumors and their normal tissues of origin. On the basis of the exceptional toxicity of fluoroacetic acid through its metabolism to fluorocitric acid and our studies on fluorinated carcinogens, Heidelberger reasoned that substitution of a fluorine atom into the 5-position of uracil might prevent its metabolism to thymidylic acid and thus interfere with DNA synthesis. He thus embarked on the synthesis of 5-fluorouracil.

Following his first studies, which showed that 5-fluorouracil inhibited the growth of a series of transplanted rodent tumors, Heidelberger enlisted the cooperation of Robert Duschinsky at Hoffman-LaRoche to perfect the synthesis of 5-fluorouracil so that tests on its therapeutic effects for tumors could be expanded. Clinical trials, first carried out at the University of Wisconsin by A. R. Curreri and F. Ansfield at Heidelberger's urging and with his cooperation, demon

[4] R. J. Rutman, A. Cantarow, and K. E. Paschkis, "Studies in 2-acetylamino fluorene carcinogenesis. III. The utilization of uracil-2-C^{14} by preneoplastic rat liver and rat hepatoma," *Cancer Res.*, 14(1954): 119-123.

strated that the new drug had clinical promise. Further studies by a number of clinical investigators have given 5-fluorouracil an important place in the chemotherapeutic treatment of several human malignancies, especially cancer of the female breast and of the colon.

In addition to 5-fluorouracil, Heidelberger's interest in fluorinated pyrimidines led to the syntheses in his laboratory of 5-fluorodeoxyuridine (which has received limited use in cancer chemotherapy), 5-fluorocytosine (clinically effective against yeast and fungal infections), and 5-trifluoromethyldeoxyuridylic acid (a tumor inhibitor that is also very active against some DNA virus infections—for example, vaccinia virus and herpes simplex, when applied locally).

Over a span of about twenty years, Heidelberger's laboratory contributed greatly to our understanding of the biochemical mechanisms of action of 5-fluorouracil and related compounds. Heidelberger observed that 5-fluorouracil is incorporated into RNA in place of uracil. However, probably the more important biological effect of 5-fluorouracil in relation to inhibition of tumor growth appears to be the powerful inhibitory activity of its metabolite 5-fluorodeoxyuridylic acid for thymidylate synthetase. He examined the mechanism of action of thymidylate synthetase and of its inhibition by 5-fluorodeoxyuridylic acid in a number of papers. Finally, one of his last scientific achievements was to develop sensitive assays for this enzyme, its normal substrate deoxyuridylic acid, and 5-fluorodeoxyuridylic acid in tumor biopsies, so that these could be studied in relation to the therapeutic responses of individual tumors to 5-fluorouracil.

These contributions to cancer chemotherapy earned Heidelberger much well-deserved recognition. His scientific deduction that 5-fluorouracil might be chemotherapeutic for cancer, his development of this idea from chemical synthesis through preclinical testing, his collaboration in the first clin ical tests, and his extensive studies on the mechanism of action of the drug attest to a scientific breadth seldom achieved.

PROFESSIONAL ACTIVITIES AND HONORS

Heidelberger spent twenty-eight years at the McArdle Laboratory, beginning as an assistant professor of oncology in 1948. He advanced to associate professor in 1952, professor in 1958, and American Cancer Society Professor of Oncology in 1960. With the development of the Wisconsin Clinical Cancer Center in 1973, he became its associate director for basic science while continuing to maintain his appointment at the McArdle Laboratory. In 1976 Heidelberger accepted the challenge of becoming the director for basic research of the Los Angeles County-University of Southern California Comprehensive Cancer Center. In this position he was responsible for organizing, recruiting new staff, and developing the overall direction of research for a new cancer center. He was named a Distinguished Professor of the University of Southern California in 1981. Although his untimely death cut short his work, Heidelberger lived to see the University of Southern California Comprehensive Cancer Center become a major center for cancer research.

Heidelberger gave generously of his time and intellect through membership on a number of professional committees and participation in symposia and meetings. He was chairman of the biochemistry committee and a member of the drug evaluation panel of the National Cancer Institute's Cancer Chemotherapy National Service Center (1958-1962); a member of the Pharmacology and Experimental Therapeutics B Study Section of the National Institutes of Health (1964-1968); a member for three terms of the board of directors of the American Association for Cancer Research (1959-1962, 1965-1968, and 1976-1979); a member of the U.S. National Committee of the International Union against

Cancer (1963-1970); twice chairman of the program committee for the American Association for Cancer Research (1960 and 1961); chairman of the program committee for the 1970 Tenth International Cancer Congress in Houston; a member of the program committee of the Eleventh International Cancer Congress in Florence, Italy, in 1974; a member of the Council of the International Union Against Cancer (1970-1974); a member of the Board of Scientific Counselors, Division of Drug Treatment, National Cancer Institute (1975-1978); a member of the fellowship committee of the International Union Against Cancer (1977-1978); a member of the fellowship committee of the International Agency for Research on Cancer, Lyon, France (1977-1978); and a member of the public issues committee of the American Association for Cancer Research (1977-1978). In 1978 he also served as a consultant to the government of the Federal Republic of Germany during their organization of the Deutsche Stiftung für Krebsforschung. In all of these activities, Heidelberger displayed a broad knowledge of cancer research and allied fields, a perceptive mind, great organizational capacity, tenacity, and willingness to work hard. He was recognized as a strong committee person who did his share of the work and expected others to do likewise.

Numerous awards came to Heidelberger for his research accomplishments: Langer-Teplitz Award for Cancer Research (1958), Lucy Wortham James Award of the James Ewing Society (1969), Walter Hubert Lecturer of the British Association for Cancer Research (1969), G.H.A. Clowes Award of the American Association for Cancer Research (1970), Annual National Award of the American Cancer Society (1974), Lila Gruber Award of the American Academy of Dermatology (1976), Papanicolaou Award of the Papanicolaou Institute for Cancer Research (1978), Founder's Award of the Chemical Industry Institute of Toxicology (1982), C. Chester

Stock Award of the Memorial Sloan-Kettering Cancer Center (1982), and Athayde International Cancer Prize of the Thirteenth International Cancer Congress (1982). Heidelberger was elected to the National Academy of Sciences in 1978. With his election, his father, Michael Heidelberger, became one of the few members of the Academy to see his child also so honored.

TEACHING

Although Heidelberger did little formal teaching, he was well known and respected as a teacher. Over the course of his career, fourteen graduate students obtained the Ph.D. degree in his laboratory and a total of eighty individuals received postdoctoral training. He taught by example in the laboratory, through critical and in-depth discussions with his students, and by means of weekly meetings of his research staff. These meetings, which usually lasted several hours on Monday evenings, included discussion of all of the research in progress in the lab. Organic chemists learned about biological problems, and biologists became familiar with discussions of synthetic organic chemistry. They all honed their critical thinking through listening and reacting to Heidelberger's probing.

Heidelberger was a master at reporting scientific meetings to his colleagues on the staff, his students, and postdoctoral associates. He returned from each meeting with detailed notes from which he could reconstruct the main argument of a speaker's report and, usually, the critical data to support the claim, and few matched his ability to sum up and convey significant points to colleagues unable to attend.

FAMILY AND SOCIAL ACTIVITIES

In an autobiography written at the end of his high school years, Heidelberger pictured himself, especially prior to high school, as a shy person. This description came as a surprise to Heidelberger's professional friends, who regarded him as strongly outgoing, somewhat aggressive, and very sociable. He enjoyed his family, and the Heidelbergers had a wide circle of friends. Their frequent social evenings might include dinner, music, and wide-ranging discussions.

Music was a highlight of Heidelberger's life. He learned to play the violin as a young boy, was a member of the Harvard symphony orchestra in college, and continued to play chamber music throughout his life. Visits from his father, an amateur clarinetist, brought evenings of chamber music with family and friends. Heidelberger was also a jazz enthusiast. He played the trumpet and drums in jazz bands while in college and maintained his membership as a jazz trumpeter in the musicians' union for much of his life. This membership enabled him to introduce himself to professional musicians and join them for a tune or two while attending professional meetings.

Heidelberger enjoyed his first visits to Europe as a young child and remained an avid traveler throughout his life. He and his wife often combined scientific meetings abroad with personal travel, making the most of the time available. He came home from England, Europe, Japan, parts of Asia, and Israel with hundreds of slides of scenery, people, and whatever else fascinated him. These slides became his props for travelogues, both in the Heidelberger home and —on several occasions—in the lecture room at McArdle.

Heidelberger's other major social activity was sailing, begun as a boyhood hobby in summer camp, nurtured during his years at Harvard, and later expanded with the purchase of a sailboat for use on Lake Mendota in Madison. His passion for sailing culminated with the acquisition of a larger boat for sailing off the coast of southern California. Sailing and enjoying music with his family and friends were the ultimate relaxation for this intensively active man.

Heidelberger was married in 1943 to Judith Werble. Their three children are Nina Heidelberger Rosefelt, Philip Heidelberger, and Lisa Heidelberger. In 1975 he married Patricia Boshell, who together with his father, children, and grandsons, Joshua Rosefelt and David Charles Heidelberger, survives him.

Heidelberger died January 18, 1983, approximately eighteen months after a diagnosis of carcinoma of the nasal sinus. During the intervening period, except for periods of intense therapy, he continued his work. As in the case of his mother's death from breast cancer in 1946, which he cited as one of his reasons for going into cancer research, Heidelberger's illness intensified his concern to find an adequate chemotherapy for cancer patients. Although he never achieved this ultimate goal, Charles Heidelberger's scientific accomplishments were impressive and earned him the recognition of his peers. His life was a full one, and he maintained strong relations with his family and friends. In his many former students and colleagues, in his research and accomplishments, Heidelberger has left a strong scientific legacy.

WE ARE INDEBTED to Michael Heidelberger for an account of Charles Heidelberger's early family life; to Patricia Heidelberger for information on his work at the University of Southern California and for an autobiography written by Charles Heidelberger at the end of his high school education; and to our colleagues at the McArdle Laboratory, especially Henry C. Pitot, Van R. Potter, and Harold P. Rusch, for making their materials on Charles Heidelberger available to us.

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The Rockefeller University

Moses Kunitz

December 19, 1887-April 20, 1978

By Roger M. Herriott

Moses Kunitz is best remembered for his isolation and crystallization of a half-dozen enzymes and precursors. This work had two important effects. First, the variety of the enzymes he isolated and the clarity of his evidence that the enzymes were proteins convinced those who had reserved judgment on the earlier reports of Sumner, Northrop, Caldwell, et al. Second, his reports of the crystallization of ribonuclease and desoxyribonuclease, which appeared just as the functions of nucleic acids were beginning to be explored, provided information on the high specificity of these enzymes. This information made them valuable tools for other researchers in their purification or the assignment of a biological function to either RNA or DNA, the two types of nucleic acid.

Moses Kunitz was born on December 19, 1887, in Slonim, Russia, where he was educated before emigrating to the United States. In 1909, he took up residence in New York City. Entering the Cooper Union School of Chemistry in 1910, he graduated with a bachelor of science degree in 1916. In the fall of that year, he entered the Electrical Engineering School of Cooper Union, where he studied until 1919 when he transferred to the Columbia University School of Mines Engineering and Chemistry. In 1922 he matricu lated as a graduate student in Columbia's Faculty of Pure Science, which awarded him a Ph.D. degree in biological chemistry in 1924.

Kunitz derived much of his formal education in graduate science from evening classes he attended while working full time as a technical assistant in Jacques Loeb's general physiology laboratory at the Rockefeller Institute for Medical Research. Loeb quickly recognized Kunitz's fine work habits and encouraged his educational development. When Kunitz received his doctorate, Loeb secured his appointment to the staff. He also collaborated with Kunitz in studies of protein-ion equilibria and related phenomena, and many of the original measurements on this subject appear in Kunitz's doctoral thesis and early publications.

Upon Loeb's death in 1924, John H. Northrop was appointed his successor. He invited Kunitz to continue with his fundamental studies of viscosity, swelling, and the effect of certain salts on the properties of proteins. Northrop joined Kunitz in many of these investigations—a happy, productive collaboration that was to last for more than thirty years.

Northrop and Kunitz moved to the Princeton branch of the Rockefeller Institute in 1926, and soon after the move, their interest shifted to the isolation of proteases. Northrop's choice of pepsin and Kunitz's choice of trypsin for these studies were due in part to the commercial availability of these substances. Although crystals of trypsin were obtained in 1931, the procedure was long and tedious, and the yield was low. In 1933 Kunitz devised a better approach. Preliminary experiments revealed that unlike the common structural tissue components, trypsinogen, the precursor of trypsin in beef pancreas, was soluble and stable in cold, quarter-normal, sulfuric acid. This information led him to develop a unique method of extracting trypsinogen and several other precursors and enzymes.

Variations of the fractions in Kunitz's assays soon revealed the presence of another protease precursor and enzyme. Because the new protease had strong milk-clotting action (a property not held by trypsin), Kunitz termed the precursor chymotrypsinogen and the enzyme chymotrypsin. In a relatively short time, Kunitz crystallized both chymotrypsinogen and trypsinogen and, soon after, the active enzymes themselves. Solubility studies that Northrop and he had developed showed these four proteins to be homogeneous. Kunitz also found conversion of trypsinogen to trypsin to be autocatalytic—that is, tryspin catalyzed the conversion. Trypsin also converted chymotrypsinogen to chymotrypsin, the kinetics in this case being first order.

Kunitz's extreme care in all of his experiments frequently led him to discoveries that the average worker might well have missed. Two instances illustrate this point. Kunitz investigated a slow change in the activity of a stored preparation of chymotrypsin that he believed to be stable. In the course of the work, he isolated two new autolysis products, still proteolytically active, which he named *beta* and *gamma* chymotrypsins, designating the original enzyme *alpha*. Again, when his trypsinogen preparation became active in acid solution—a result contrary to his earlier studies—he discovered that his stock HCl solution was contaminated with a mold that liberated a protease that had brought about the activation. He isolated the mold and then the mold protease. He then used the protease to convert trypsinogen to trypsin in an acid medium, obtaining a cleaner preparation of trypsin than was possible by any previous procedure.

The presence of substances inhibitory to trypsin in the original pancreatic extracts, and in certain soybean meal fractions, led Kunitz to the crystallization of a polypeptide inhibitor from the pancreas and a protein inhibitor from soybean. Isolation of the inhibitor from the pancreas answered a ques tion Kunitz had already posed: Why does trypsinogen remain inactive in pancreatic tissue when the pH is optimal for its activation?

Kunitz's interests, however, were far broader than merely the isolation of enzymes or inhibitors. In each instance, he studied the interaction of the inhibitor with the enzyme and isolated the complexes, studying their stoichiometry and other properties. One of his finest papers details the study of the kinetics and thermodynamics of the reversible denaturation of the soybean trypsin inhibitor.

From 1939 to 1940, Kunitz worked to isolate ribonuclease from beef pancreas. He found it to be one of the smallest proteins and extremely stable—even to boiling. This enzyme liberates only pyrimidine mononucleotides from ribonucleic acids. The isolation of desoxyribonuclease came ten years later, after Maclyn McCarty had obtained its partial purification. Very low (nanogram) levels of this enzyme destroyed the pneumococcal transforming activity of Avery, MacLeod, and McCarty's DNA preparations—a finding that led many investigators to believe that DNA carried hereditary determinants.

With the onset of World War II, when the laboratory's attention was focused on government projects, Kunitz was asked to isolate hexokinase, thought to be highly sensitive to the action of a poison gas. He isolated the hexokinase in crystalline form, but had to isolate three other crystalline proteins before the hexokinase crystallized.

The following anecdote reveals Kunitz's remarkable faculty for crystallizing proteins. Another laboratory had devoted considerable effort to the isolation of a plant protein of great interest to the Department of Defense, but the investigator had been unable to crystallize the protein. A package of the material was sent to Kunitz with the request that he attempt to crystallize it. The package arrived late one afternoon. Kunitz dissolved some of the dry powder in water and placed small aliquots in a series of test tubes to which he added drops of dilute HCl, increasing the number of drops in each successive tube. A precipitate soon began to appear in the middle of the series, and Kunitz held a turbid tube to the light from the window, remarking, after a few moments, "It looks granular." He placed the tubes in the refrigerator, and the next morning several tubes had crystals of what proved to be the active protein.

It is unfortunate that more beginning investigators did not get the chance to work near Kunitz in the early years. Margaret McDonald and this author were certainly enriched by our long association with him. After his return to New York in 1952 and the conversion of the Rockefeller Institute to its present university status, Kunitz was named professor emeritus and continued to work daily in the laboratory. Many staff and students then had an opportunity to see how the master worked.

Kunitz's papers, models of scientific reporting, also illustrate his reliance on the results of broad experimentation rather than on preconceived notions. His procedures of exposing proteins to strong acid or high temperatures—unique at that time—were avoided by most investigators.

There is no more appropriate testimony to the esteem in which Kunitz was held by his peers than the comments of John Northrop, which were included in a review of Kunitz's work when he was awarded the Carl Neuberg Medal in 1957: "Dr. Kunitz possesses to a rare degree the abilities of a research worker of the first rank in his chosen field—imagination, ingenuity, persistence, great technical skill, mathematical facility, and a thorough theoretical knowledge. It is not surprising, therefore, that he has been able to solve almost every problem he has attempted. Some of them are of great importance. The isolation and crystallization of ribo nuclease, hexokinase, and deoxyribonuclease placed the protein nature of enzymes, in general, on a firm experimental foundation. In addition, the nucleases have been invaluable tools in the elucidation of the chemistry of the nucleic acids, those remarkable substances that appear to be the very 'stuff of life'."

Moses Kunitz was a modest, gentle, considerate person who loved his work and his family. His association with the Rockefeller Laboratories spanned a period of fifty-seven years. He died April 20, 1978, in Philadelphia, Pennsylvania. He is survived by a daughter, Roslyn Albert, and a son, Jacques Kunitz.

HONORS AND DISTINCTIONS

Moses Kunitz was associated with The Rockefeller University for almost sixty years (1913-1972). He was elected associate member in 1940, member in 1949, and professor emeritus in 1953. Kunitz was awarded the American Society of European Chemists and Pharmacists (New York City) Carl Neuberg Medal in 1957. He was elected to the National Academy of Sciences in 1967 and received an honorary degree from The Rockefeller University in 1973. He was a member of the American Association for the Advancement of Science, the Society for Experimental Biology, the American Society of Biological Chemists, and the Society of General Physiologists.

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Orren Jack Turner

Robert Helmer MacArthur

April 7, 1930-November 1, 1972

By Edward O. Wilson and Evelyn G. Hutchinson

In November 1972 a brief but remarkable era in the development of ecology came to a tragic, premature close with the death of Robert MacArthur at the age of 42," wrote Martin Cody and Jared Diamond in the 1975 memorial volume, *Ecology and Evolution of Communities*.

MacArthur will be remembered as one of the founders of evolutionary ecology. It is his distinction to have brought population and community ecology within the reach of genetics. By reformulating many of the parameters of ecology, biogeography, and genetics into a common framework of fundamental theory, MacArthur—more than any other person who worked during the decisive decade of the 1960s—set the stage for the unification of population biology.

MacArthur was the youngest son of John Wood MacArthur, a professor of genetics at the University of Toronto and Marlboro College in Vermont. After completing his undergraduate education at the latter institution and taking a master's degree in mathematics at Brown University, Robert MacArthur took a Ph.D. in 1957 at Yale University, under the direction of G. Evelyn Hutchinson. In order to receive additional training in field ornithology, he spent the academic year 1957-1958 with David Lack at Oxford University. Hutchinson, Lack, and an older brother, the physicist John

W. MacArthur, Jr., were dominant influences in shaping MacArthur's unique blend of mathematical and ecological interests. From 1958 to 1965, MacArthur advanced from assistant professor to full professor at the University of Pennsylvania. He then moved to Princeton University, where he ended his career as Henry Fairfield Osborn Professor of Biology. In 1952 he married Elizabeth Bayles Whittemore, with whom he had four children (Duncan, Alan, Elizabeth, and Donald).

MacArthur began his career with three articles that revealed an unusual power and originality of approach. The first (1955) was the proposal of a way to measure community stability taken from information theory, formalizing for the first time a concept that, until then, could only be expressed through verbal description.

Soon afterward (1957) came the celebrated "broken-stick" model of the relative abundance of bird species. Although the specific hypothesis of competition embodied in the broken-stick distribution has been disputed and the approach was later dismissed as obsolete by MacArthur himself, we should not overlook the real significance of this contribution, which did indeed appear to describe what happens in nature in some as yet imperfectly studied circumstances. In three short pages, MacArthur audaciously confronted a central problem of community ecology that previous writers had scarcely formulated in words. He characterized the issue in such a way as to suggest that the deepest remaining mysteries of natural history can be reached by leaps of the imagination—so long as such efforts are disciplined by the postulational-deductive method.

Reviewers sometimes forget that the broken-stick hypothesis was only one of three frequency distributions presented in the article, each derived from a different, competing set of biological hypotheses. The method of multiple working hypotheses was thereby introduced to this branch of ecological theory. The 1957 article set the tone for all of MacArthur's later work. Inevitably, his approach was condemned by some ecologists as oversimplification, but—right or wrong in particular applications—it energized a generation of young population biologists and transformed a large part of ecology.

MacArthur's third early contribution was an elegant analysis of niche division in warblers (1958). For this somewhat more conventional study, he received the Mercer Award of the Ecological Society of America. The warbler study revealed the real secret of MacArthur's success, his almost unique status as a mathematician-naturalist. He was a mathematician of professional grade, having been trained in the discipline before commencing the formal study of ecology. He shared the conviction of pure mathematician G. H. Hardy, whom he resembled very much in temperament and philosophy, "that a mathematician was a maker of patterns of ideas, and that beauty and seriousness were the criteria by which his patterns should be judged."

In conversation, MacArthur would say that the best science comes, to a great extent, from the creation of *de novo* and heuristic classification of natural phenomena. "Art," he enjoyed quoting Picasso, "is the lie that helps us to see the truth." But MacArthur was also a born naturalist. He watched birds with the patience and skill of a professional ornithologist, visited the tropics as often as he could, and delighted in the endless facts of natural history, which were temporarily exempted from his cartesian scalpel. The store of random information thus accumulated and the shadowy play of its many patterns were the real inspiration of his theoretical work.

The decade of the 1960s was a period of intense activity for Robert MacArthur. While serving on the faculty of the

University of Pennsylvania and then at Princeton, he began a parallel series of investigations, many in collaboration with colleagues and students, that touched on a wide range of topics around the central problem of species diversity. Part of his special genius was an ability to work closely with persons of widely varying talents and interests, to turn them into fast friends, and to bring out the best in their scientific labors. One of them, E. O. Wilson, who coauthored this memoir, recorded the following impression of him:

> He was medium tall and thin, with a handsomely angular face. He met you with a level gaze supported by an ironic smile and widening of eyes. He spoke with a thin baritone voice in complete sentences and paragraphs, signaling his more important utterances by tilting his face slightly upward and swallowing. He had a calm understated manner, which in intellectuals suggests tightly reined power. Because very few intellectuals can keep their mouths shut long enough to be sure about anything, MacArthur's restraint gave his conversation an edge of finality he did not intend. In fact he was basically shy and reticent. He was not a mathematician of the first class—very few scientists are, otherwise they would become pure mathematicians—but he joined superior talent in that field with an extraordinary creative drive, decent ambition, and a love of the natural world, birds, and science, in that order.[1]

MacArthur and his coworkers analyzed the evolution of the demographic parameters, established the environmental correlates of bird diversity, and formulated and partly solved the species packing problem. One of his most influential works, *The Theory of Island Biogeography* (1967), written with Wilson, created species equilibrium theory. This theory explored the many ramifications of a balance of species number on islands and on "habitat islands," any sharply demarcated habitat—such as a lake, or even, for insects at least, a tree in

[1] E. O. Wilson, *Biophilia* (Cambridge, Massachusetts: Harvard University Press, 1984), p. 68. A further account of MacArthur's collaborative work and its impact on ecology has been given by Sharon E. Kingsland in *Modeling Nature: Episodes in the History of Population Ecology* (Chicago: University of Chicago Press, 1985).

the middle of a field. During colonization, the extinction rate in species/unit time rises as the number of species on the island rises and the immigration rate falls. When the two converge, a dynamic equilibrium is attained in which the continuing turnover varies according to the speed with which the colonization took place. The models predict an increase in species numbers with larger island area and greater proximity to the mainland. Other investigators have added many refinements to this basic theory. Experimental tests have also been performed on isolated habitats, from bottles of nutrients to full-scale islands and island habitats in the Florida Keys and the Brazilian Amazon.

The current theory of island biogeography, while still very inadequate for the largest and most complex systems, has worked well enough to become an important part of both ecology and biogeography. It is also a cornerstone of the new field of conservation biology because of its relevance to the study of the extinction process and the planning of natural reserves.

As time passed MacArthur spoke of himself increasingly as a biogeographer and made the subject the focus of his teaching at Princeton. In 1971, when he learned he had only a year or two left to live, he quickly brought the many threads of his work together in the single book, *Geographical Ecology: Patterns in the Distribution of Species*. The clarity and incisiveness of this synthesis show him at the height of his power. *Geographical Ecology* is both the reflective memoir of a senior scientist and the prospectus of a young man whose creative effort ended at the point of its steepest trajectory.

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December 16, 1901-November 15, 1978

By Clifford Geertz

Margaret Mead was probably the most famous anthropologist of her time, and even more probably the most controversial. Author of more than fifteen hundred books, articles, films, and occasional pieces; a tireless public speaker traveling the world to instruct and persuade; a field researcher of extraordinarily extensive and varied experience; a hyperactive organizer of projects, conferences, programs, and careers; and possessed of a seemingly endless fund of opinions on every subject under the sun that she was all too willing to share with anyone who asked, and many who did not; she left no one who came into contact with her or her works indifferent to either.

Even death, which came from pancreatic cancer in the winter of 1978, a month shy of her seventy-seventh birthday, did not still the debates that circulated about her person and her work. The appearance in 1983 of the New Zealand/Australian anthropologist Derek Freeman's highly publicized wholesale attack on her first book, *Coming of Age in Samoa*, published fifty-five years earlier, began yet another round of intense and often bitter discussion, both popular and professional, whose end is still not in sight. She was the subject of a special memorial issue of the *American Anthropologist* in June 1980, in which eight of her students and coworkers contrib uted assessments of various aspects of her work; of an affecting memoir by her daughter, Mary Catherine Bateson, herself an anthropologist, in 1984; and of a mammoth, fact-crammed popular biography by Jane Howard, also in 1984. The following memoir is heavily dependent upon these latter works, supplemented—even colored, perhaps, for they are very vivid—with certain remembrances of my own.[1]

THE CAREER

For all the complexity of her person and the variety of her interests, Mead's biography is fairly simply told, for once she found her path—in the early 1920s—she never diverged from it. Impulsive, improvisitory, peripatetic, she may have been, as well as socially unorthodox, but she led a directed life, willed and implacable.

She was born in Philadelphia in December 1901, the first of five children, to Emily Fogg and Edward Sherwood Mead. Her father was a professor of economics at the Wharton School of Finance of the University of Pennsylvania. Her mother had been a schoolteacher before marriage (and subsequently did some work toward a master's degree in sociology), as had been her paternal grandmother, Martha Ramsay Mead, who lived with the family during Mead's childhood. After a Quaker elementary school education in Philadelphia

[1] *American Anthropologist*, 82,2 (1980):261-373; Mary Catherine Bateson, *With a Daughter' Eye* (New York: Morrow, 1984); Jane Howard, *Margaret Mead, A Life* (New York: Simon and Schuster, 1984). For a full bibliography, missing only the last few years, and with an introduction by Mead on her writings, see *Margaret Mead: The Complete Bibliography 1925-1975* , ed. Joan Gordan, (The Hague: Mouton, 1976). For a sensitive appreciation from outside anthropology, see Renée Fox, "Margaret Mead," *International Encyclopedia of the Social Sciences* (New York: The Free Press, 1979). Of the numerous newspaper obituaries, the fullest is that by Alden Whitman of *The New York Times*, November 16, 1978. Mead's own account of her early life is available as *Blackberry Winter: My Earlier Years* (New York: Morrow, 1972).

It should also be remarked that the inordinate delay in the appearance of this memoir is a result of the fact that I was asked to write it only after the person to whom it was originally assigned failed at length to produce it.

and public high school in nearby Doylestown, Mead attended DePauw University, Greencastle, Indiana. She actively disliked DePauw and left after a year to transfer to Barnard College. She majored in psychology at Barnard, ultimately writing a master's essay on intelligence testing of Italian and American children. For her doctoral work she moved, in 1923, into anthropology at Columbia University under Franz Boas and Ruth Benedict, writing a library theis on cultural stability in Polynesia. In 1925—despite the misgivings of her teachers and most of her friends—she travelled, aged twenty-three, alone and enervated, to Samoa for her first field trip.

In a pattern that she was to repeat several times and indeed never wholly abandon, two works—one popular, tendentious, schematic, and over-discussed; one technical, detached, detailed, and generally neglected—resulted from this nine-month field study: *Coming of Age in Samoa* (1928) and *The Social Organization of Manu'a* (1930). In 1928-1929 Mead worked in Manus in the Admiralty Islands off the north coast of New Guinea for eight months, from which came the popular *Growing Up in New Guinea* (1930) and the technical *Kinship in the Admiralty Islands* (1934). After a summer's work among the Omaha Indians in Nebraska in 1930 (from which a study, *The Changing Culture of an Indian Tribe* [1932] resulted with the usual immediacy, though in this case with rather little impact, public or professional), Mead journeyed to New Guinea, where she worked among three different groups—the Tchambuli (or Chambri), the Mundugumor (or Biwat), and the Arapesh—between December 1931 and spring 1933. Again, two major works resulted: one for the world, argumentative and controversial, *Sex and Temperament in Three Primitive Societies* (1935), and one for the trade, systematic and not much noticed, *The Mountain Arapesh* (1938-1949). From March 1936 to March 1938, plus another six weeks in 1939, Mead worked in Bali, The Netherlands

East Indies, producing perhaps her finest single study, the essay in *Balinese Character: A Photographic Analysis*, Bateson and Mead (1942). Finally, in 1953, she conducted a six-month restudy of Manus, which emerged in 1956 as *New Lives for Old: Cultural Transformation—Manus 1928-1953*. Various short revisits to her sites aside (she made at least a half-dozen of them between 1964 and 1975 alone, and nearly twenty altogether), Mead thus carried out nearly six years of extensive field research in no less than seven cultures—all of them except Bali and the transformed Manus, neolithic; all save the Omaha, in the South Pacific—and wrote substantial books (and numerous articles) about all of them. It is a record, like Malinowski's monograph *Fleuve* or Frazer's galactic compilation, unlikely to be broken.

Not that she was otherwise idle while accomplishing this. As early as 1926 she was appointed assistant curator of ethnology of the American Museum of Natural History in New York, a position she maintained (advancing to associate curator in 1942; curator in 1964; and curator emerita, but hardly retired, in 1969) until her death, and whose obligations as collector, documentor, conservator, and exhibition designer she took extremely seriously. She added upwards of three thousand items to the Museum's inventory, planned several dioramas, made hundreds of photographs and a number of films, raised (and, not insignificantly, contributed) funds, and finally created, apparently by sheer insistence, ("this has been part of my own working life for forty-five years"[2]) the splendid Peoples of the Pacific Hall, which opened there in 1971.

Although it took Columbia University until 1954 to bring itself to make her an adjunct professor, she also taught: at

[2] D. H. Thomas, "Margaret Mead as a Museum Anthropologist," *American Anthropologist*, op. cit., p. 357, an excellent review of this rather little known aspect of Mead's career.

Vassar in 1939-1940, 1940-1941, 1945-1946; at New York University in 1940, and from 1965 to 1967; at Wellesley in 1944; at The Menninger Foundation in 1959; at Columbia from 1947 to 1951, in 1952-1953, and from 1954 to 1978; at Fordham University from 1968 to 1970; and at the University of Rhode Island in 1970-1971. She was, *inter* a great many *alia*, Jacob Gimbel Lecturer in the Psychology of Sex, at Stanford University and the University of California (1946); Mason Lecturer, University of Birmingham, England (1949); Inglis Lecturer, Graduate School of Education, Harvard University (1950); Ernest Jones Lecturer, British Psychoanalytic Society (1957); and Dwight Terry Lecturer on Religion in the Light of Science and Philosophy, Yale University (1957). During the Second World War she lectured at the Office of War Information and afterwards at UNESCO and the National Institute of Mental Health. How many student groups, women's clubs, alumni associations, and professional organizations she addressed will probably never be known.

Beyond field research, curating, and teaching, Mead was a tireless organizer and director of an astonishing variety of intellectual and social enterprises. The list of her "memberships" in a curriculum vitae apparently prepared a year or so before her death ("Full material is provided so that each one can select the particular items relevant for his or her purpose") runs to eighty-four items, from Parents Without Partners, Spirit of Stockholm Foundation, National Council for Negro Women, and General Board of Examining Chaplains of the Episcopal Church to Anthropological Film Research Institute, World Federation for Mental Health, Society for Psychical Research, and The Association for Social Anthropology in Eastern Oceania. She served no less than twenty-six of these groups in some sort of executive capacity. She was, at various points, president of The Society for Applied

Anthropology (1949), The American Anthropological Association (1960), and The American Association for the Advancement of Science (1975).

She was the moving force in the Research in Contemporary Cultures program at Columbia from 1948 to 1950, in which more than 120 people, including Ruth Benedict, Geoffrey Gorer, Nathan Leites, Martha Wolfenstein, and Rhoda Metraux, participated, and from which a number of her own "national character" studies, notably *Soviet Attitudes Toward Authority* (1951) and (with Metraux) *Themes in French Culture* (1954), emerged. By the time she was finished, she was covered with honors, including twenty-eight honorary degrees (Delhi, Kalamazoo, Harvard, Lincoln, Women's Medical College of Pennsylvania . . .), the Viking Medal in Anthropology (1957-1958), and, in 1975 (rather late, she thought, as did a great many others) fellowship in The National Academy of Sciences. In 1977 she was admitted to the American Philosophical Society. In 1979 she was posthumously awarded The Presidential Medal of Freedom.

Mead was married three times: first, in 1923, to Luther Cressman, a theological student, from whom she was divorced in 1928; second, in 1928, to the New Zealand anthropologist Reo Fortune, with whom she worked in Manus, among the Omaha, and on New Guinea, and from whom she was divorced in 1935; and third, in 1936, to the English anthropologist Gregory Bateson, with whom she worked in Bali and New Guinea, and from whom she was divorced in 1950. All three of her husbands survived her, as did her daughter, Mary Catherine Bateson Kassarjian, at the time of her mother's death, dean of social sciences at Reza Shah Civar University in Iran; a granddaughter, Sevanne Kassarjian; and one of her sisters, Elizabeth Mead Steig. When she died, the people of Manus rested seven days in mourning and planted a coconut tree.

THE WORK

As with any scholar who produces so vast and varied an output, no simple verdict is possible concerning the overall quality of Mead's work. Some of it was clearly hasty, ill-considered, and casually argued, even irresponsible. Some of it was routine, banal, momentarily useful at best, page-filling at worst. Some of it was professional, careful, a modest but genuine addition to knowledge. And some of it was extraordinarily fine, revolutionary when written and revolutionary still. It is doubtful that any anthropologist, save perhaps she herself, ever has read or ever will read everything, even everything professional, she wrote (certainly, I have not); but any anthropologist, in any way serious, has read and for some time to come will read some of it. She started a great many hares and she caught a number of them.

Even an attempt to demarcate the major areas, beyond Oceanic ethnography as such, in which Mead made her main contributions is likely to prove controversial, for she had a way of making everyone from nutritionists to cinematographers feel that their interest was at the very center of her concern, before all others. Nevertheless, from a detached perspective, four areas seem to be those upon which the durability of her reputation will ultimately rest: psychological anthropology; applied anthropology; ethnographic method; and a complex of concerns centering around gender roles, child socialization, and the family, which now would perhaps be called women's studies, a categorization she would have found, and toward the end of her life increasingly did find, constrictive.

Psychological anthropology was a major theme in her work from her first full-scale field study—of the Samoans in the mid-1920s, concerned as it was with undermining the *Sturm und Drang* conception of adolescence—to her last, the return to Manus in the mid-1960s, where the subject was "[the] strange emergence of a group of erstwhile savages twice upon the world stage, once unconscious of their role, now fully aware of it" (*New Lives for Old*, 186), and the subject of one of her very last papers, a retrospective summary piece published posthumously in 1979, "The Evocation of Psychologically Relevant Responses in Ethnological Field Work" (in ed. G. Spindler, *The Making of Psychological Anthropology* , pp. 88-139. Berkeley: University of California Press).

There were essentially three overlapping phases of this work: first, that represented by *Growing Up in New Guinea*, with its attack on fixed stages of cognitive growth (the children were "realists," the adults "animists"), as well as by the Samoan study, in which proposed universalities of psychological functioning were up-ended by particular counter-cases; the second, usually referred to as "culture and personality" research, in which particular cultural mechanisms (teasing, swaddling) were sought out to account for particular psychological traits (affectlessness, suppressed rage); and the third, usually referred to as "national character" work, in which entire societies (Russian, French, American) were characterized in psychological terms (paranoid, reserved, optimistic). If the first of these suffered from a tendency toward thesis driving, the second from a rather mechanical conception of the relation between child socialization and adult character, and the third from a certain over-ambitiousness, taken together they established, especially in the Manus, Balinese, and American studies, the foundations for virtually all subsequent work in this area.

The second area, applied anthropology, was in many ways Mead's dominant concern, determined as she was to make her science serve human needs. It took her into a large number of government-related "policy science" activities, including the direction, as executive secretary, of The Committee on Food Habits of the National Research Council during World War II. Her concern continued after the war and contributed to the enactment of the Child Nutrition Act of 1978. Five days before her death she sent a "Dear Jimmy" telegram to President Carter from her hospital bed urging him to sign it.

Her practical interests pervade all her work and determine its fundamental direction. Race conflict, child care, marital relations, women's rights, technological development of Third World countries, mental health, education, drug abuse, the generation gap, American foreign policy, environmentalism, aging, and nuclear disarmament all came—and repeatedly—under her gaze, half-ethnographic, half-moralist, entirely passionate. And (some rather too quotable remarks aside), she had useful things, novel and challenging, nicely provocative, to say about all of them. Her foundation, in 1944, of The Institute of Intercultural Studies, to "stimulate . . . research . . . most likely to affect intercultural and international relations," and to which she dedicated the greater part of her sizeable income, is only the clearest expression of the centrality of the applied dimension in Mead's conception of what she was about: "building a new world . .. through a disciplined science of human relations" (*Balinese Character*, xvi).

Mead's concern with methodological matters was with her from the beginning, intellectual daughter of Franz Boas that she was, but it was powerfully stimulated by attacks on her, as she became prominent, as "impressionistic," "intuitive," "subjective," and, to her the most painful cut of all, "unscientific." Mead was totally committed (as her other mentor, Ruth Benedict, for example, was not) to the view that anthropology was or ought to be a science, pure and simple, just like the others. Most of her methodological discussions and enterprises came in reaction to accusations that it, or anyway she, was anything less than thoroughly objective, logically rigorous, resolutely empirical. ("Each time I write something about 'how I really do it'," she once complained to me, "'they' use it to show that I'm not to be trusted.")

With a candor and bravery not otherwise matched in social anthropology—and certainly not by her whitecoated critics, who tend to shoot at her from behind one way mirrors—Mead continuously exposed her field procedures to full view and evaluation (her papers deposited in the Library of Congress—letters, field notes, manuscripts; a half-million items in all—probably constitute the fullest and most open record of an ethnographer's work practices extant). Her search for new and better methods was relentless.

At various points she experimented with several forms of psychological testing—projective, Piagetian, IQ; with the analysis of children's play and children's paintings; with hyper-behaviorist, timed observations ("There are two sorts of anthropologists," she once said, pointedly, to me, "'talking' anthropologists and 'looking' anthropologists: I'm a 'looking' anthropologist."); with life-history recording; with modes of language learning and language use; and perhaps most extensively with photography and with that original combination of documentary research, film analysis, expatriate interviewing, and literary study that she called "culture at a distance."

Some of these efforts were more successful than others. Even Gregory Bateson was, or so at least he said to me, unconvinced of some of Mead's claims for the probative value of their photographic work. Even a sympathetic observer must cock a quizzical eye at the oddly phrased claim (in her *vita)* that "she has had to learn to use seven primitive languages"; and projective testing is not much now in fashion. But the vigor with which she pursued the most intractable problems of ethnographic method and the great impact her experiments and reflections have had upon research practice in general are hardly to be denied.

As for the complex of issues centering around the family, socialization, gender roles, and the status of women, they were more deeply rooted in Mead's unusually complex personal life than any other aspect of her work: in her relation to her mother, her grandmother, her sisters, her daughter, and her granddaughter; in her college-formed, lifelong friendships with a number of extraordinarily talented professional and artistic women; in her long-term, deeply intimate relationship with Ruth Benedict; in her earliest investigations into the erotic freedom of Samoan girls, the marital dominance of Tchambuli women, and the emotional inconstancy of Balinese mothers. Finally—in her ambiguous relations in the last years of her life with the reborn feminist movement in the United States—Mead was acclaimed by some as a heroine who had made it in a man's world on her own terms. Yet she was derided by others as a "Queen Bee" and an "Aunt Tom" who (as Betty Friedan, an *ennemie amicale* for many years, told Joan Howard) "played a considerable role in getting us all so preoccupied with 'fulfillment.'" Professionally, the culmination of this concern was her 1949 *Male and Female*, with its *vive la difference*, to each his or her own, point of view. But all in all she probably wrote more on marriage, family, gender, sexuality, childhood, and child-raising than on any other set of issues—much of it influential, most of it controversial, all of it heartfelt.

THE PERSON

Trying to sum up Margaret Mead in a few considered and professional pages is, for someone who knew her, if not intimately at least live and in color, a bit like trying to inscribe the Bible—or perhaps the *Odyssey*—on the head of a pin. She escapes most categories and mocks the rest.

My own most vivid memories are two. The first is of going with my then wife, Hildred Geertz, to see her in 1950, when she was at the height of her celebrity, in the famous tower in the American Museum to ask whether a philosophy major and an English major from a small Ohio college where the subject was not even taught ought to become anthropologists. Although she did not know of us before (the appointment had been arranged by one of those, also famous, young women she collected about her in the tower as aides of all-work, who happened to be a friend of ours), she spent the entire afternoon showing us her notes, photographs, project outlines, telling us about the field (and some of the leading personalities in it!), extolling its possibilities for free spirits such as we imagined ourselves to be, and practically commanding us to enter it. We left commanded.

The other memory is from seven years later. My wife and I, journeymen now, are in a very small village on the Balinese coast, so remote it cannot be reached by automobile. We have been there for a week or so observing a gigantic cremation being held by some relatives of the family with whom we were living. At the climax of this extravaganza—my wife is up by the palace where the procession will begin, I am down toward the burning ground a half mile away where it will end, in a desperate attempt to "cover" it—the enormous, tumbling crowd, hundreds of people half-shrouded in heat and dust, suddenly parts, as in a deMille movie, and there standing, leaning authoritatively on a stick, is Margaret Mead. I thought: "If an anthropologist goes mad in the field, this is the way it will happen—hallucinating Margaret."

I didn't even approach her but went to find my wife ("Come and look. You're not going to believe this") so as to have a reality check on what I thought I was seeing. Reassured it was indeed she, we then went up to her. She was *en route* to India for some sort of World Conference on some sort of World Problem, had gone to where we were permanently staying, found out where we had gone, had walked in on her notoriously bad ankles in the mid-day heat to find us. She apologized: She knew anthropologists don't like other anthropologists to intrude into their field sites. She had come only to invite us to dinner, three days hence, in the island capital, where there was a local Javanese art dealer married to a Balinese, whom she had known for years and whom it would be good for us to meet. We accepted. She departed, hobbling back to the main road where her car was waiting. The dinner was as useful as promised; and, by the then deserted Sanur beach (Sukarno was about to throw the Dutch out and virtually all Europeans had left the island), Margaret quietly asking, the art dealer even more quietly answering, we silently listening, strange and beautiful.

The cliché with which memorials of this sort used ritually to end was, "We shall not look upon her like again." For my part, I am absolutely astonished (and wildly grateful) that she ever existed in the first place. So, too, the field should be.

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David Nachmansohn

March 17, 1899-November 2, 1983

By Severo Ochoa

David Nachmansohn's scientific lifepath was strongly influenced by his early studies on the biochemistry of muscle in Otto Meyerhof's laboratory. This experience led to an interest in the biochemistry of nerve activity, a field of study to which he would devote most of his scientific life. In so doing, he contributed—perhaps more than any other investigator—to our understanding of the molecular basis of bioelectricity.

David Nachmansohn was born in Jekaterinoslav, Russia (now Dnjetropetrowsk, USSR). His parents came from middle-class families among whom were many lawyers, physicians, and other professionals. Before David and his two sisters reached school age, the family moved to Berlin where they had many relatives. Thus, David's background and education were essentially, if not exclusively, German. His college education was strongly humanistic, with Latin, Greek, literature, and history as mainstays, some mathematics, and the rudiments of physics. Through his readings, perhaps primarily through his reading of the second part of Goethe's *Faust* when he was only seventeen years of age, he became interested in philosophy—so much so that he continued to attend courses and seminars in philosophy even while a medical student at Heidelberg in 1920.

When he entered the University of Berlin in the spring of 1918, David was strongly oriented toward the humanities. After Germany's defeat in World War I, however, the newly established republic faced grave social, political, and economic problems, and David was advised to study medicine, a profession that could provide economic independence. He accepted this advice and became a medical student; but as time went on, he became more and more interested in biology through his avid readings about the lives and scientific accomplishments of Bernard, Pasteur, Helmholtz, Ehrlich, and others. Eventually, he decided to devote his life to biomedical research and after his graduation in 1924 joined the laboratory of Peter Rona at the Charité for training in biochemistry.

The Charité was the university hospital of Berlin University Medical School in whose Department of Pathology Rona directed a division of biochemistry. There, Nachmansohn joined an exceptional company of bright young people: among them, Fritz Lipmann, Hans Adolph Krebs, Rudolph Schoenheimer, Ernst Chain, Karl Meyer, and Hans H. Weber. Nachmansohn's first paper, "Vital Staining and Adsorption," was published in collaboration with Krebs, an endeavor that began a lifelong friendship between the two. Nachmansohn also did some collaborative work with Weber that led to the publication of a paper entitled, "The Independence of Protein Hydration and Ionisation."

At Rona's, he became familiar with the work of the great Dahlem biochemists Meyerhof, Warburg, and Neuberg, which he found fascinating. Weber advised Nachmansohn to go to Otto Meyerhof at the Kaiser-Wilhelm Institut für Biologie in Berlin-Dahlem for further training. But when Nachmansohn approached Meyerhof, the eminent researcher informed him abruptly that he did not accept beginners—a position he reversed after speaking with the young Nach mansohn awhile. In Meyerhof's laboratory, Nachmansohn's postdoctoral contemporaries included Fritz Lipmann, Hermann Blaschko, Francis O. Schmitt, and this author. Karl Lohmann, who later discovered ATP, was Meyerhof's assistant, and Dean Burk was a visiting scientist. Hans Krebs was also in the same building, in Otto Warburg's laboratory. Nachmansohn often mentioned that it was Meyerhof who had had the most profound impact on his later work and scientific outlook.

Nachmansohn joined the Meyerhof laboratory in 1926. At that time, Grace and Philip Eggleton at the Cambridge biochemical laboratory had recently discovered a new phosphorylated compound in muscle they called "phosphagen" because it liberated inorganic phosphate during contraction. Soon thereafter, Fiske and Subbarow at Harvard Medical School showed the new compound to be phosphocreatine in which phosphate is linked to creatine through a phosphoamide bond.

During this period, Meyerhof was interested in the energetics of muscular contraction. He worked to determine, as he had previously with various hexose phosphates, the heat of hydrolysis of phosphocreatine. It proved to be very high—of the order of 10,000 to 12,000 calories per mole—which contrasted with the low heat of hydrolysis of hexose phosphates (1,500 to 3,000 calories per mole). This finding enabled researchers to distinguish between high- and low-energy compounds in metabolism. (Some years later, it was shown that the breakdown of ATP to ADP and inorganic phosphate was the energy-yielding process more immediately related to muscular contraction, whereas the breakdown of phosphocreatine served to resynthesize the ATP. Lactic acid formation, most of which took place after contraction, was—like phosphocreatine breakdown—a recovery process aimed at restoring rapidly the relatively small ATP stores of resting muscle. Finally, the glycogen that gave rise to the lactic acid was resynthesized from lactic acid using the energy released by oxidation of a fraction of the lactic acid produced).

These developments fascinated the young David Nachmansohn and greatly influenced his later work.[1] During his early years in Meyerhof's laboratory, the function of phosphocreatine was unknown, and interest in this compound was very strong. It is therefore not surprising that Nachmansohn was given the assignment of looking for the relations among phosphocreatine breakdown, lactic acid formation, and the tension developed by muscle during isometric contraction in anaerobiosis. He also compared the phosphocreatine content of different kinds of muscle, especially muscles differing in the rapidity of their contraction. He found that rapidly contracting muscles contained much more phosphocreatine than slowly contracting ones, a fact that was consistent with, and in a way foretold, the function of phosphocreatine in muscular contraction.

Nachmansohn vividly described the atmosphere at Dahlem in the 1920s[2] when several Kaiser-Wilhelm research institutes were concentrated in a relatively small area: the Institute of Physical Chemistry, with Haber, Ladenburg, Polanyi, Freundlich, and Bonhoeffer; the Institute of Chemistry, with Beckman, Willstätter, Otto Hahn, and Lise Meitner; the Neuberg Institute of Biochemistry; and the Institute of Biology, with Meyerhof, Warburg, Goldschmidt, Correns, and Hartmann. The young Nachmansohn was particularly stimulated by the "Haber Colloquia" in which Fritz Haber, the discoverer of the process for conversion of nitrogen and hydrogen into ammonia, attempted to bridge the

[1] Nachmansohn described these influences in an unpublished manuscript entitled "Molecular Aspects of Bioelectricity: An Autobiography."

[2] David Nachmansohn, "Molecular Aspects of Bioelectricity"; "Biochemistry As Part of My Life," *Annual Review of Biochemistry* 41(1972):1-27.

gap between physicists, chemists, and biologists so as to promote better understanding and cooperation among them. Nachmansohn credited these monthly colloquia, which were regularly attended by many members of the various institutes, with having greatly expanded his scientific and spiritual horizons.

Like so many others of Jewish origin, Nachmansohn left Germany when Hitler came to power. He was offered the opportunity of working at the Sorbonne, and in 1933 established himself in Paris with his wife, Edith, and their baby daughter, Ruth. From Paris, Nachmansohn made several visits to London, only a few hours away, to attend meetings of the British Physiological Society. As he explained in the 1972 autobiographical article in the *Annual Review of Biochemistry*, he could never have anticipated that, by attending those meetings, his scientific interests would take a new, unexpected turn. He could also not have predicted that this new turn would determine the direction of his scientific work for the rest of his life.

At that time, one of the main topics of discussion in the London meetings was the role of acetylcholine in nerve activity. Following the pioneering work of Otto Loewi and of Dale and his colleagues, Dale proposed that acetylcholine acts as a transmitter of nerve impulses across junctions (synapses) between neurons or between nerve and muscle, in contrast to the electric currents that propagate impulses along nerve and muscle fibers. This idea was supported by two main lines of observations: (1) the release of acetylcholine at synaptic junctions, as judged by its appearance in the perfusion fluid of certain ganglia, or striated muscle motor endplates, upon electrical stimulation of the afferent nerves; and (2) the powerful stimulating action of acetylcholine when applied locally to synaptic junctions, which was in striking contrast to its failure to elicit a response when applied to nerve fibers.

Acetylcholine was known to be rapidly hydrolyzed by an enzyme, acetylcholine esterase, which is strongly inhibited by the alkaloid, eserine. In fact, no acetylcholine was found in the perfusion fluid of stimulated ganglia unless the fluid contained eserine, an indication that the acetylcholine released by electrical stimulation was rapidly hydrolyzed.

It seemed to Nachmansohn that much more knowledge was needed on the nature, distribution, and concentration of acetylcholine esterase in various tissues and that such information might provide clues to the role of this enzyme in nerve activity. He began work on this problem in Paris in 1936 and soon found that acetylcholine esterase was present at high concentrations in many different types of excitable fibers of nerve and muscle and in brain tissue, in both vertebrates and invertebrates; it was hardly detectable, however, in such organs as the liver or kidney. In addition, the concentration appeared to be several-fold higher at the neuromuscular junctions than in the nerve fibers.

In his study of the literature on the neuromuscular junction, Nachmansohn came across an article by J. Linhard in which the electric organs of fish were described as modified muscle fibers, comparable to motor endplates, in which the muscular elements were either missing or present only in rudimentary form. He thought it would be of interest to determine the acetylcholine esterase content of electric tissue. Nachmansohn had happened to see live *Torpedo* at the 1937 Paris World's Fair; he managed to procure some for study and found the concentration of acetylcholine esterase in the electric organ to be exceedingly high. In his own words, "The result was simply stunning: 1 g of electric tissue (fresh weight) hydrolyzed 3-4 g of acetylcholine per hour, although the tissue is 92% water and only 3% protein."[3]

[3] David Nachmansohn, "Biochemistry As Part of My Life," *Annual Review of Biochemistry* 45(1972): 1-27.

The importance of this discovery, which opened the way for the elucidation of the molecular mechanisms involved in the generation of bioelectricity, can hardly be overestimated. In collaboration with Egar Lederer, Nachmansohn soon used the electric organ of the *Torpedo* fish to purify acetylcholine esterase. (This work was reported in a 1939 paper published in the *Bulletin de la Société de Chimie Biologique* [*Paris*].) In addition, Nachmansohn carried out experiments on the same organ in June 1939 at the Marine Biological Station at Arcachon, near Bordeaux. Together with W. Feldberg (a pharmacologist from Dale's group) and A. Fessard (an electrophysiologist at the Sorbonne), Nachmansohn provided the first unequivocal evidence for the electrogenic action of acetylcholine; the results were published in 1940 in the *Journal of Physiology*.

His next paper on electric tissue, prepared in collaboration with C. W. Coates and R. T. Cox, was published from Yale in 1941 in the *Journal of General Physiology*. This paper dealt with the correlation between the electrical potential and the acetylcholine esterase content of different sections of the electric organ of the electric eel. The use of electric tissue later made possible the crystallization and biochemical characterization of acetylcholine esterase in Nachmansohn's laboratory as well as the isolation of choline acetylase and the acetylcholine receptor.

In 1939, John Fulton invited Nachmansohn to join his department at Yale University. He stayed in New Haven until 1942, when he moved to Columbia University and became associated with the Departments of Neurology and Biochemistry at the College of Physicians and Surgeons. In New Haven, he had already begun to work with the electric organ of the electric eel (which he obtained from the New York Aquarium) and found not only that the acetylcholine esterase concentration was as high as in *Torpedo* but that the electric tissue contained phosphocreatine and ATP in concentrations comparable to those in striated muscle. Furthermore, the electrical discharge was accompanied by phosphocreatine breakdown. These observations suggested to him that the energy required for resynthesis of the acetylcholine hydrolyzed during the electrical discharge was supplied by the same processes that provide the energy required for muscular contraction, namely ATP and phosphocreatine breakdown, lactic acid formation, and, in the last instance, carbohydrate oxidation.

Soon after Nachmansohn moved to Columbia, he tested the idea that electric tissue contains enzymes capable of utilizing the energy of ATP for the acetylation of choline, an idea that indeed proved to be the case. This was, in many respects, key because it was the first time that ATP was found to drive a synthetic reaction other than through phosphorylation. Nachmansohn soon found that choline acetylase, the enzyme(s) responsible for the acetylation reaction, required a coenzyme because the activity of the acetylase-containing extracts was lost after dialysis and was restored by the addition of boiled enzyme. The identity of this coenzyme remained obscure, however, until Lipmann and coworkers found that an enzyme catalyzing the formation of acetylsulfonamide from ATP, acetate, and sulfonamide also required a coenzyme (coenzyme A, or CoA for short) for activity. They elucidated the structure of this coenzyme in 1947.

The discovery of choline acetylase was published by Nachmansohn and Machado in the *Journal of Neurophysiology* in 1943. Ironically, three journals (*Science, Journal of Biological Chemistry*, and *Proceedings of the Society for Experimental Biology and Medicine*) refused to publish this eminent and trailblazing biochemical paper. The reviewers apparently could not believe that ATP would participate in reactions other than phosphorylations. In retrospect, they cannot be blamed for their skepticism because Nachmansohn's finding was totally unexpected. Acetylation was eventually found to result from the coupling of two reactions: (1) ATP + acetate + CoA → AMP + inorganic pyrophosphate + acetyl-CoA; and (2) acetyl CoA + choline (or sulfonamide) → CoA + acetylcholine (or acetyl-sulfonamide).

Work proceeded in a number of laboratories on the localization of acetylcholine esterase using biochemical assays (e.g., of the extruded axoplasm and the sheath of the giant axon of the squid) and electron microscopic observations. The results of these studies made it appear highly probable that the enzyme was a component of excitable membranes everywhere-not only of synaptic membranes but also of the membranes of axons and conducting fibers in general. In his Harvey Lecture entitled "Metabolism and Function of the Nerve Cell" (delivered in 1953 and published in 1955), Nachmansohn advanced the view that acetylcholine acts as a signal recognized within the membrane by an acetylcholine receptor protein; this results in a conformational change that leads to increased local permeability to ions and membrane depolarization, thus generating an action potential-an idea that proved to be correct. Ernest Schoffeniels, in Nachmansohn's laboratory, was able to isolate the electroplax, the single-celled elementary unit of electric tissue, which was found to be extremely rich in acetylcholine esterase and receptor protein.

If one considers that receptors are now recognized as the initial elements in the response of all cells to specific stimuli and that the concept originated with the acetylcholine receptor, it becomes evident that Nachmansohn set a biological landmark. This was also the first neurotransmitter receptor to be characterized biochemically, thanks to its accessibility in the vertebrate muscle endplate and its abundance in the specialized electric organ of electric fish.

The finding that acetylcholine esterase activity is very high in excitable membranes—including nerve fiber membranes—and that the localization of the acetylcholine receptor is the same as that of the esterase led Nachmansohn to postulate that the nerve impulse is generated through a depolarization of the membrane by acetylcholine released by the stimulus from an inactive complex with protein. The action potential thus generated would give rise to the release of acetylcholine in adjacent sites leading to propagation of the current along the fiber by successive acetylcholine bursts. Rapid hydrolysis of acetylcholine by the esterase and the ion pump mechanism coupled to the breakdown of ATP would restore membrane polarization at each point as the impulse travelled down the fiber.

Nachmansohn's theory, already suggested in earlier publications, was presented in detail in his book, *Chemical and Molecular Basis of Nerve Activity*, first published in 1959. A revised edition appeared in 1975 with considerably more experimental support for his ideas. The revised edition also contained two supplements, one by Nachmansohn on the properties and functions of proteins of the acetylcholine cycle in excitable membranes and one by E. Neumann that presented a molecular model for bioelectricity.

Nachmansohn's ideas, however, were not accepted by neurophysiologists. His molecular theory of nerve conduction is still highly controversial, despite the fact that a variety of experiments by Nachmansohn and others (detailed in the 1975 edition of his book) would appear to nullify objections to his theory. The fact, for instance, that acetylcholine when applied locally stimulates at synaptic junctions or motor endplates but has no effect on axons, may be explained by impermeability of the intact axonal membrane to quaternary ammonium ions. Acetylcholine, therefore, stimulates axons when applied at the Ranvier node sites where the myelin sheath is much thinner. It also stimulates when applied to areas of a nerve fiber where the phospholipids of the myelin sheath have previously been hydrolyzed by treatment with phospholipase. By the same token, curare—which competes with acetylcholine for binding to the receptor—blocks transmission of the nerve impulse across synapses but does not affect conduction when applied locally to the surface of nerve fibers. It does, however, block conduction when applied at Ranvier nodes or to the surface of fibers previously treated with phospholipase.

Physostigmine (eserine), a tertiary ammonium base, and prostigmine, a quaternary ammonium base, are both inhibitors of acetylcholine esterase, and the former—but not the latter—can depress conduction when applied to a single frog sciatic nerve fiber. Moreover, the excitable membrane of certain axons (e.g., those of the walking leg of the lobster) appears to be incompletely protected; these axons can be stimulated by the local application of acetylcholine. Organophosphates such as diisopropylfluorophosphate (DFP) or tetraethylpyrophosphate (TEPP) are irreversible inhibitors of acetylcholine esterase and block conduction across synapses and along nerve fibers.

Both the inhibition of acetylcholine esterase and the conduction block can be reversed by pyridine-2-aldoxime (PAM)-an organophosphate antagonist developed in Nachmansohn's laboratory by Irving Wilson as a war gas antidote. (It may be mentioned parenthetically that organophosphates are used commercially as insecticides. PAM has found a nonmilitary application in the systemic treatment of insecticide poisoning. Some local anesthetics are structural analogs of acetylcholine and compete with the latter for receptor binding, blocking electrical activity in the conducting and synaptic parts of excitable membranes.

Despite these results, the current belief is that the acetyl choline system is intercellular and not intracellular. Acetylcholine is thought to be liberated only at cholinergic nerve endings in the synaptic cleft and to bind to the receptor on the postsynaptic side, functioning, therefore, exclusively as a synaptic transmitter. Axonal conduction is believed to involve primarily electric field effects on conformational transitions of protein-ion channels. The high concentration of acetylcholine esterase and acetylcholine receptor in axonal membranes is nevertheless a remarkable fact that remains unexplained.

Nachmansohn's work attracted a great number of students and investigators, and his laboratory at the College of Physicians and Surgeons was for many years a place of much excitement and feverish activity. Nearly four hundred papers, the majority original research papers, were published from his laboratory between 1947 and 1977. In addition, Nachmansohn was an indefatigable traveler and lectured extensively in the United States and abroad.

In the spring of 1980, former students, collaborators, and friends of David Nachmansohn organized an international symposium at the University of Liège to honor him on his eighty-first birthday.[4] It was apparent at this meeting that the field of endeavor he had pursued so vigorously for many years had been expanded in many directions by his former associates and their students. Particularly noteworthy was the tremendous progress in our knowledge of the molecular structure of acetylcholine esterase and of the acetylcholine receptor.

The importance of Nachmansohn's acetylcholine receptor

[4] *Molecular Aspects of Bioelectricity: Festschrift and Proceedings of the International Symposium and Poster Session in Honor of David Nachmansohn on the Occasion of his 81st Birthday, Liège, May 25-27, 1980 under the Auspices of the Université de Liège, Belgium, and the Max-Planck-Institut für Biochemie, Martinsried, München, Germany* . Ed., Ernest Schoffeniels and Eberhard Neumann. Oxford: Pergamon Press, 1980.

idea for our understanding of the generation of bioelectricity in molecular terms may be gauged from the review by Changeux (a former collaborator with Nachmansohn) and his associates,[5] and a recent report[6] prepared for the National Institute of Mental Health by panels of scientists in various areas of neurobiology and related fields. In these publications, the monomeric form of the receptor is described as a transmembrane, allosteric protein with an approximate molecular weight of 250,000, containing two acetylcholine (agonist) binding sites and consisting of four types of polypeptide chains of apparent molecular weights: 39,000 (α), 48,000 (β), 58,000 (γ), and 64,000 (δ) in a ratio of $\alpha_2,\beta,\gamma,\delta$. The receptor has several functional states: In the resting state, it has low affinity for agonists, and the ion channel is closed; in the active state, the binding sites are occupied by agonist and the channel is open. On binding two molecules of acetylcholine, the receptor undergoes rapid transitions (on a submillisecond time scale) between the resting and the active state. These fluctuations last a few milliseconds until hydrolysis of the acetylcholine causes its dissociation from the receptor.

After his retirement in 1967, Nachmansohn continued to work, travel, and lecture extensively. He was an enthusiastic supporter of the Zionist cause and made many visits to Israel. He was very active on behalf of the Hebrew University and the Weizmann Institute and was for many years a member of the board of governors of the latter institution. Nachmansohn was a firm believer in the world fraternity of science and was among the first scientists of German-Jewish origin to visit Germany after the war, working with strong determination for the reestablishment of scientific ties between

[5] J.-P. Changeux, A. Devillers-Thiéry, and P. Chemoulli, "Acetylcholine Receptor: An Allosteric Protein," *Science* 225(1984):1335-45.

[6] *The Neuroscience of Mental Health*. U.S. Department of Health and Human Services Publication no. (ADM)84-1363. Rockville, Md.: 1984.

Germany and the West. He also promoted intensely scientific rapprochement between Germany and Israel. In the 1970s Nachmansohn devoted himself to the study of the role played by German-Jewish scientists in the explosion of scientific knowledge that took place in the first quarter of this century. This effort culminated in the publication of his book, *German-Jewish Pioneers in Science: 1900-1933*.[7]

Because of his interest in art and history, David Nachmansohn was a stimulating travel companion. My wife and I enjoyed his company on many a visit to Israel, Italy, Sicily, and Greece, profiting from his scholarly knowledge of the classical world. David had strong convictions and defended them stubbornly, but he never let scientific preoccupations interfere with his enjoyment of life. He was refined in his tastes and gentle and understanding with his friends.

I am greatly indebted to Arthur Karlin (Columbia University) and Jean-Pierre Changeux (Institut Pasteur) for helpful suggestions.

[7] David Nachmansohn, *German-Jewish Pioneers in Science: 1900-1933* (New York: Springer, 1979).

HONORS

Nachmansohn became a member of the National Academy of Sciences in 1965. He was also a member of the American Academy of Arts and Sciences, the German Academy of Natural Sciences (Leopoldina), and an honorary member of the Weizmann Institute of Sciences of Israel and the Berlin Medical Society. He was a recipient of the Pasteur Medal (Paris), the Neuberg Medal (New York), the Medal of the Société de chimie biologique (Paris), the Albrecht von Graefe Medal of the Berlin Medical Society, the Nicloux Medal (Paris), and the Gold Medal of the Spanish Council for Scientific Research. He received an honorary M.D. degree from the Free University of Berlin and honorary D.Sc. degrees from the University of Liège (Belgium) and Tufts University (Boston).

An international symposium on the molecular basis of nerve activity was held at the Free University of Berlin, in October 1984, in memory of David Nachmansohn. That this symposium was sponsored jointly by the Max-Planck-Gesellschaft zur Forderung der Wissenschaften, the Société française de chimie biologique, the Weizmann Institute of Sciences, the Deutsche Forschungsgemeinschaft, the Senator for Science and Research of the City of Berlin, the Free University of Berlin, and the Gesellschaft für Biologische Chemie, attests to the high esteem in which David Nachmansohn was held by his colleagues and friends.

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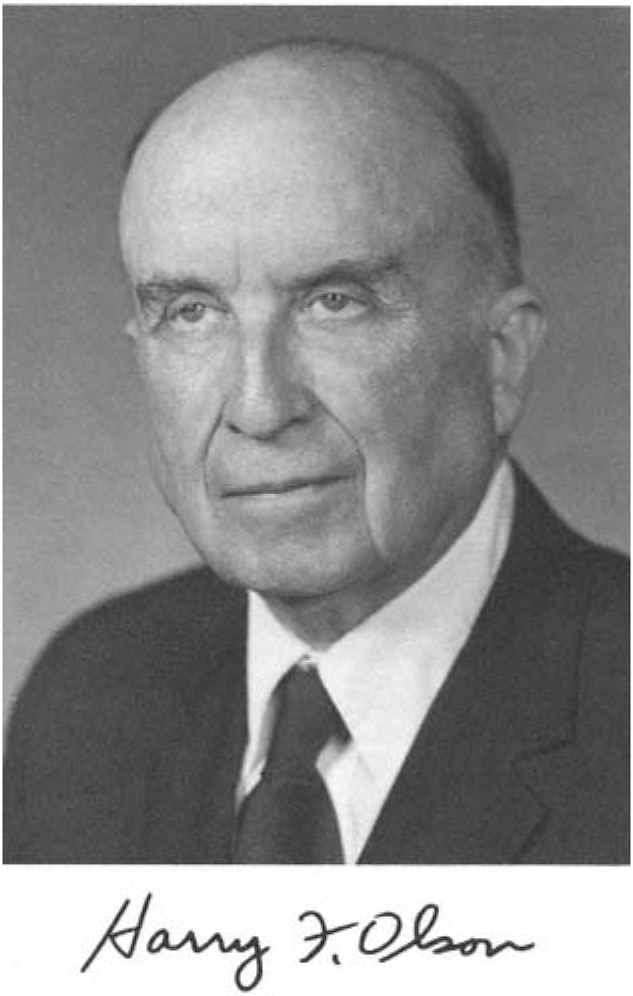

Harry F. Olson

December 28, 1901-April 1, 1982

By Cyril M. Harris

Harry F. Olson, pioneer in acoustics and electronic sound recording, died on April 1, 1982, at Princeton Medical Center at the age of eighty-one. He had been a member of the National Academy of Sciences since 1959.

During his career of nearly forty years with RCA, Dr. Olson developed several types of microphones for broadcasting and recording, high-fidelity loudspeakers, phonograph pickups and recording equipment, underwater sound equipment, and sound motion picture and public address systems; he contributed substantially to the development of the RCA magnetic tape recorder for television and the RCA music synthesizer.

Harry F. Olson was born in Mt. Pleasant, Iowa, on December 18, 1901, the first of two children. Both his father, a farmer, and mother, a talented amateur artist, were born in Sweden and had come to this country to seek new opportunity.

Their son exhibited an interest in science and technology at an early age, which they encouraged by supplying him with a modest shop and laboratory. While still in grade school and with very little data on design, Harry built and flew model airplanes-an art then in its infancy. In high school he graduated to building a steam engine and a wood-fired boiler, which he used to drive a direct current generator constructed from parts of an automobile generator he had rewound for 110 volts. He also designed and built an amateur radio station, became proficient with the code, and obtained an operator's license.

In 1924, majoring in electrical engineering, Harry graduated near the top of his class from the University of Iowa's College of Engineering. G. W. Stewart, then head of the physics department, chose him to receive a graduate scholarship, and in 1925, he earned the M.A. degree with a thesis on acoustic wave filters in solids. As part-time research assistant to J. A. Eldridge, he worked on polarization of light by electron impact; while with A. Ellett he conducted research on atom beams.

One experiment, verifying the Maxwell velocity distribution of atoms, used a small boiler partially filled with cadmium and equipped with a narrow aperture to supply a fine beam of atoms. The atom beam was sent through a series of Fizeau wheels driven by the squirrel-cage rotor of an induction motor, all operating in a vacuum. The three-phase stator windings of the induction motor were located outside the vacuum chamber. The atom beam passed through the slots in the wheels and the atoms were collected on a glass plate cooled by liquid air. They then measured the density of the collected atoms. From the dimensions, geometry, rotational velocity, and density, the researchers determined the velocity distribution. They then reflected a narrow beam of cadmium atoms from a rock salt crystal and found that the reflection was specular. For his doctoral thesis, Olson carried out research on the polarization of resonance radiation in mercury and received the Ph.D. degree in 1928.

From his association with Stewart, the inventor of the acoustic wave filter, and with Dean Carl E. Seashore, who specialized in the psychology of music, Harry Olson devel oped an interest in music, acoustics, and sound reproduction. In 1928, he joined RCA as a member of the Research Department. Except for the two-year period from 1930 to 1932, when he was associated with the Engineering Department of the Photophone Division of RCA in New York City, Dr. Olson was associated with the RCA research organization continuously until his retirement. In 1934 he was placed in charge of acoustical research for the RCA Manufacturing Company. In 1942 his Acoustical Research Laboratory was moved from Camden, New Jersey, to the newly constructed RCA Laboratories in Princeton, New Jersey, where he had a well-equipped acoustical facility, constructed under his supervision. This included a free-field (anechoic) room that was the world's largest at that time, a reverberation chamber, and an ideal listening room. He continued as director of acoustical research until 1967, when he was appointed staff vice-president.

Dr. Olson's work on the development of microphones for the motion picture and broadcast industries resulted in microphones that found widespread commercial use. Especially noteworthy were his bidirectional velocity microphones and his unidirectional cardioid microphones. He continued to develop new types of microphones, including higher-order gradient microphones, ultra-directional microphones, noisecancelling microphones, and various types of miniature microphones which were used both in industry and in the military. He also developed loudspeakers that made significant improvements in linearity and uniformity in frequency response of loudspeakers that were commercially available at the time.

During World War II, Dr. Olson and the group he led worked on various military projects with an emphasis on underwater sound and antisubmarine warfare. This work included significant improvements in sonar transducers, the development of an acoustic proximity fuse for depth charges, and voice communication transducers for use in noisy environments. During the academic years from 1940 to 1942, he also lectured in acoustical engineering at Columbia University.

Following World War II, Dr. Olson continued his research in sound reproduction. One of his experiments, now considered a classic, determined the preferred bandwidth for the reproduction of music. Previous experimenters had found that listeners seemed to prefer a high-frequency cutoff of 5000 Hz for reproduced music. Dr. Olson carried out an experiment in which a small orchestra sat behind a visually opaque but acoustically transparent screen. The screen incorporated a concealed low-pass acoustical filter having an upper frequency cutoff of 5000 Hz. This filter could be opened or closed, allowing either the full range of frequencies to pass or the range only below 5000 Hz. The listeners were asked to select their preference between two conditions: full bandwidth or restricted bandwidth. There was overwhelming preference in favor of the full bandwidth. Next, the orchestra was replaced with a sound-reproduction system where the loudspeakers were located in the position of the orchestra, behind the screen. When the sound system was free of distortion, the listeners preferred the full bandwidth. But when he introduced small amounts of nonlinear distortion, the restricted bandwidth was preferred, thus demonstrating clearly the importance of high quality in audio systems.

Early in 1950, RCA asked Dr. Olson to develop a team in his laboratory to make significant improvements in magnetic tape recording that could lead to the magnetic tape recording of television signals. To accomplish this would require a breakthrough in the quality of both the magnetic tape and the recording heads. The 3M Company was selected as the collaborator for providing the special tape needed for this new process. In May 1956, after several years of development, the system was completed and was moved from his laboratory in Princeton to the NBC Studios in New York City, where it provided the world's first broadcast of tape-recorded color television signals. Dr. Olson then started a project in tape-coating technology in his laboratory. When finally developed, this equipment was transferred, as a unit, to RCA's newly created Magnetic Products Division in Indianapolis, where it was used in the commercial production of magnetic tapes.

Dr. Olson's interest in musical acoustics led to the development, with Herbert Belar, of the RCA Electronic Music Synthesizer. Music synthesizers have become commonplace since the advent of transistors and integrated circuits. But in the era of vacuum tubes and relays, of which the RCA device was constructed, the production of an arbitrarily selected audio signal by means of a synthesizer was a considerable achievement. At first, Olson and Belar's synthesizer was used at the RCA Laboratories at Princeton to compose musical selections that were issued as records. It was later moved to the Electronic Music Center at Columbia University, where it is still in use.

For his achievements, Dr. Olson received many honors and awards, including the Modern Pioneer Award of the National Association of Manufacturers (1940), the John H. Potts Medal of the Audio Engineering Society (1952), the Samuel L. Warner Medal of the Society of Motion Picture and Television Engineers (1955), the John Scott Medal of the City of Philadelphia (1956), the Achievement Award of the IRE Professional Group on Audio (1956), the John Ericsson Medal of the American Society of Swedish Engineers (1963), the Emile Berliner Award of the Audio Engineering Society (1965), and the Institute of Electrical and Electronic Engi neers' Mervin J. Kelly Medal (1967), Consumer Electronics Award (1969), and Lamme Medal (1970).

He was awarded the first Silver Medal in engineering acoustics of the Acoustical Society of America in 1974 and in 1981 was given the Gold Medal of the Society with the following citation: "... for his innovative and lasting contributions in acoustic transduction, sound reproduction, electronic music and speech synthesis, and his service to the Society." He served on the Executive Council of the Society from 1937 to 1940, as vice-president from 1942 to 1944, president-elect from 1951 to 1952, and president from 1953 to 1954. He was, in addition, associate editor of the *Journal of the Acoustical Society of America* for thirty years.

He was a member of the American Society of Motion Picture and Television Engineers, Fellow of the American Physical Society, Fellow of the Institute of Electrical and Electronic Engineers, and Fellow of the Acoustical Society of America. Dr. Olson was an honorary member, a founder, and past-president of the Audio Engineering Society. He was also a member of Tau Beta Pi and Sigma Xi and received an honorary D.Sc. degree from Iowa Wesleyan College.

Dr. Olson was the author of numerous acoustical studies and contributed to more than 130 articles and professional papers. His books, *Elements of Acoustical Engineering* (1940, 1947), *Dynamical Analogies* (1942, 1958), *Musical Engineering* (1952), *Acoustical Engineering* (1957), and *Music, Physics and Engineering* (1966), are widely used by students and engineers throughout the world. *Acoustical Engineering* and *Dynamical Analogies*, particularly, are considered standard reference texts in the field and have been translated into Russian and Japanese. Dr. Olson held more than one hundred U.S. patents awarded on devices and systems in the field of acoustics, a partial list of which follows. The titles given here are descriptive and are not the actual titles recorded on the patents.

Many of his patents are considered to be fundamental—as, for example, patents on the velocity microphone, the cardioid microphone, functional sound absorbers, the electronic music synthesizer, the air-suspension loudspeaker, and the electronic sound absorber.

Harry Olson retired in 1967 but continued as a consultant to RCA Laboratories for several years thereafter. He is survived by his wife, the former Lorene Johnson of Morris, Illinois, whom he married in 1935. In their early years, Lorene helped him to prepare the manuscripts for his many books and articles. Like his mother, she was an amateur artist, and her prominently displayed oil paintings enlivened his office walls throughout his career.

HONORS AND DISTINCTIONS

Degrees And Honorary Degrees

1924 B.E., University of Iowa
1925 M.S., University of Iowa
1928 Ph.D., University of Iowa
1932 E.E. (Professional), University of Iowa
1959 D.Sc. (Honorary), Iowa Wesleyan

Memberships

Tau Beta Pi
Sigma Xi
Acoustical Society of America, Past-President
Audio Engineering Society, Past-President
Society of Motion Picture and Television Engineers
Institute of Electrical and Electronic Engineers
American Society of Swedish Engineers
American Physical Society
National Academy of Sciences

Honors And Awards

1940 Modern Pioneer Award of the National Association of Manufacturers

1952 John Potts Gold Medal of the Audio Engineering Society

1955 Samuel L. Warner Gold Medal of the Society of Motion Picture and Television Engineers

1956 The John Scott Medal of the City of Philadelphia

1956 The Achievement Award of the Institute of Radio Engineers

1963 John Ericsson Gold Medal of the American Society of Swedish Engineers

1965 The Emile Berliner Award

1967 Mervin J. Kelly Medal of the Institute of Electrical and Electronic Engineers

1969 Consumer Electronics Award of the Institute of Electrical and Electronic Engineers

1970 Lamme Gold Medal of the Institute of Electrical and Electronics Engineers

1974 The First Silver Medal of the Acoustical Society of America

PATENTS

1932	Velocity Microphone	1,885,001
1932	Unidirectional Cardioid Microphone	1,892,645
1935	Double Voice Coil Loudspeaker	2,007,748
1940	Multiple Flare Horn	2,203,875
1941	Line Microphone "Shotgun Microphone"	2,228,886
1942	Multiple Loudspeakers	2,269,284
1949	Air Suspension Loudspeaker	2,490,466
1950	Synthetic Reverberation	2,493,638
1950	Functional Sound Absorbers	2,502,016
1951	Single Element Cardioid Microphone	2,539,671
1953	Noise Discriminator, Threshold Type	2,645,684
1958	Electronic Music Synthesizer	2,855,816
1961	Speech Analyzer	2,971,058
1961	Electronic Sound Absorber	2,983,790
1961	Music Composing Machine	3,007,362
1963	Stereophonic Loudspeaker	3,104,729
1964	Stereophonic Disk System	3,118,977

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With R. A. Hackley. Combination horn and direct radiator loudspeaker. Proc. Inst. Radio Eng., 24 (12):1557.
A unidirectional microphone. J. Soc. Motion Pict. Eng., 27(3):284.
1937 Horn loudspeakers, part 1. RCA Rev., 1(2):68.
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Oscar Knefler Rice

February 12, 1903-May 7, 1978

By Benjamin Widom and Rudolph A. Marcus

With the death of Oscar Rice at Chapel Hill, North Carolina, in the spring of 1978, physical chemistry lost one of its foremost practitioners, a man who for more than half a century had been a leader and an inspiration in the development of that science. For the last forty-two of those years he had been a member of the chemistry faculty of the University of North Carolina, as Kenan Professor from 1959 and as Kenan Professor Emeritus from 1975. He died the week before he was to have been awarded an Sc.D. degree by his university. The degree was awarded posthumously; he was cited as "very likely the most distinguished chemist ever to have lived in North Carolina."[1]

Oscar Rice was born in Chicago on February 12, 1903. His parents, Oscar Guido Rice and Thekla Knefler Rice, had been married only six months when his father died of typhoid fever. His mother never remarried, and Oscar never knew a father. He was brought up by his mother and her sister, Amy Knefler, who joined them as homemaker while Thekla Rice supported the household as a secretary. Although the financial resources of the family were strained,

[1] Maurice M. Bursey, *Carolina Chemists: Sketches from Chapel Hill* (Department of Chemistry, University of North Carolina at Chapel Hill, 1982), p. 153.

Oscar's mother and aunt made the sacrifices necessary to enable him to complete his education.[2]

Oscar attended what was then San Diego Junior College (now San Diego State University) from 1920 to 1922, then transferred to the University of California, Berkeley, where he was awarded the B.S. degree in 1924. He stayed on at Berkeley for his graduate studies and by 1926—he was then only 23 years old—had earned his Ph.D. (Two of his contemporaries as graduate students at Berkeley were Henry Eyring and Joseph E. Mayer, also to become important figures in physical chemistry.) After one more year at Berkeley (1926-27) as an Associate in Chemistry, Rice became a National Research Fellow.[3] He spent the first two years of his fellowship, 1927 to 1929, at the California Institute of Technology (with brief stays again in Berkeley); the third, 1929-30, was spent in Leipzig.

On his return from Leipzig, Rice was appointed Instructor in Chemistry at Harvard. He had by then already completed the early versions of his great work on the theory of unimolecular reactions, written at Berkeley and Caltech, so it can hardly have been a surprise when, in 1932—after having been at Harvard for two years—he was given the second American Chemical Society Award in Pure Chemistry. (The first winner, in 1931, was Linus Pauling.) For some years while at Harvard, Rice gave a course of lectures entitled "Advanced Inorganic Chemistry" on which he later based his book *Electronic Structure and Chemical Binding*. The book was not completed, however, until 1939, after Rice's first three years in Chapel Hill. It was published in 1940.

Rice's Harvard period was highly productive on the research side. He studied energy exchange in inelastic molec

[2] From a letter by his wife, Hope Sherfy Rice, to their friend "Cally" (the Reverend Ann Calvin Rogers-Witte), written May 10, 1978, three days after Oscar Rice's death.

[3] In later years called a National Research Council Fellow.

ular collisions, using creatively the methods of what was then the new quantum mechanics. He continued the work on unimolecular reaction-rate theory and on predissociation and diffuse spectra, which he had begun earlier at Caltech and Leipzig. He wrote his noted papers with Gershinowitz (a Harvard graduate student and a Parker Traveling Fellow at Princeton) on reaction-rate theory, and he pursued his important experimental work on thermal decompositions with the collaboration of D. V. Sickman (a postdoctoral associate), A. O. Allen (his first graduate student), and H. C. Campbell.

Although those years at Harvard could hardly have been more fruitful, Rice seemed not to be very happy there. A. O. Allen believes that the social sophistication of Harvard may not have been well suited to Rice's quiet, solitary, and contemplative style. Later, at Chapel Hill, he found him to be more relaxed and at peace—although otherwise unchanged.[4]

On leaving Harvard in 1935, Rice returned briefly (1935-36) to the Berkeley chemistry department as a research associate. In 1936, with an appointment as associate professor, he began his long and illustrious career at the University of North Carolina at Chapel Hill. He was promoted to full professor in 1943.

Rice was to remain at Chapel Hill, although he traveled widely for conferences and lectures and took an occasional leave of absence. Just after the Second World War, from 1946 to 1947, Rice took a position as Principal Chemist at the Oak Ridge National Laboratory. "The story goes that the Army officer in charge of the laboratory was much concerned about the productivity of this man who sat all day in an armchair thinking. When it was time to review what had been produced, the quality of the work that Dr. Rice had generated in the armchair was so impressive that the officer recom

[4] Letter of November 8, 1982, by A. O. Allen to the authors.

mended stuffed armchairs for every scientist whom he supervised."[5] Before that, at Chapel Hill, under contract to the Office of Scientific Research and Development, Rice had worked on the problem of the burning of rocket powders (1950g).[6] In 1947 he was awarded a U.S. Army and Navy Certificate of Appreciation for his war research.

It was at Oak Ridge that Oscar Rice met Hope Ernestyne Sherfy, whom he asked to join him as his wife when he returned to Chapel Hill. They were married in 1947. Hope Rice was Oscar's constant companion and a source of joy, comfort, and support for their more than thirty years together. They adopted two daughters, Margarita and Pamela, both born in Germany. The Rices adopted them on two separate trips Oscar (accompanied by Hope on the first one) made to Germany to attend scientific congresses. After the death of Oscar's Aunt Amy, his aged mother came to live with them in a new and larger house they built in Chapel Hill.

The only substantial time Rice spent away from the University of North Carolina, except for his year at Oak Ridge, was in 1968, when he was a visiting professor at the Virginia Polytechnic Institute (now the Virginia Polytechnic Institute and State University) in Blacksburg, and in 1969, when he was Seydel-Woolley Visiting Professor of Chemistry at the Georgia Institute of Technology.

Those physical scientists who, like Oscar Rice, were born in the first half of the century's first decade, reached scientific maturity along with the new quantum theory and wave mechanics. They could thus, still as young men, participate in the glorious crusade that caused one after another famous problem of physics or chemistry to yield to the power of the new ideas and techniques. Writing of the time he began re

[5] Bursey, *Carolina Chemists*, p. 151.

[6] Here and hereafter, years and letters in parentheses refer to entries in the appended bibliography; thus, (1950g) means the seventh entry for 1950.

search with Rice at Harvard, A. O. Allen says: "Oscar had just recently published his epochal paper with Ramsperger on the theory of unimolecular reactions, which played an important role in the expansion of physical chemistry during what I later heard H. S. Taylor refer to as the 'glorious thirties.' Indeed, a time when the rest of the world was depressed and fearful was just when the physical sciences were most exciting and hopeful. I asked for nothing better than to join the exciting revolution in chemical dynamics under Oscar's tutelage."[7]

Rice's first work at Berkeley was not with quantum mechanics, for the new theory had hardly been born. Instead, he investigated those aspects of colloid stability and surface tension that could be treated by classical methods. In his first published paper (1926a), he acknowledges help from R. C. Tolman of Caltech and J. H. Hildebrand of Berkeley, who were, or were soon to be, recognized as two of the most prominent physical chemists and inspiring teachers in this country. At Berkeley, Rice also knew G. N. Lewis, who held the promising young student in high regard and later recommended him for the faculty position at Harvard.[8] Rice's early work on surface tension was to have important echoes later in his career. Indeed, the combining of microscopic with macroscopic, largely thermodynamic, ideas to create a phenomenological theory or description—the process one sees in these early papers—was also to be the style of much of his later work from the 1940s on.

His great work on unimolecular reactions was also, at first (1927b), non-quantum mechanical. It followed and was intended to explain the measurements of H. C. Ramsperger (also then in the Berkeley chemistry department) on the de

[7] A. O. Allen letter.

[8] As attested by a longtime friend, Professor Milton Burton of Notre Dame, in a letter of November 4, 1983, to the authors.

composition of azomethane. Presumably, it was during Rice's first postdoctoral year, when he was still at Berkeley as an Associate in Chemistry, that he and Ramsperger formulated the theory.[9]

The general problem was accounting for the rates of unimolecular decompositions or isomerizations, particularly for the observed fall-off of the rate at low pressures. Earlier ideas of Lindemann, later elaborated by Hinshelwood (both worked in England), yielded some important clues. A primitive version of that early theory is the following: Suppose A is the molecule that will react to form product P, and that it does so through a high-energy intermediate A* that is formed by the collision of A with some species M that could be either A or some chemically inert gas with which A is diluted. The reaction scheme is then:

$$A + M \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A^* + M, \qquad A^* \xrightarrow{k_2} P,$$

characterized by activation and deactivation rate constants k_1 and k_{-1} and by the rate constant k_2 for reaction of the activated species. If the population of the latter is assumed to vary only slowly during the reaction (the "steady-state" approximation), the apparent rate coefficient k for the observed reaction A → P is

$$k = k_1 k_2 (M) / [k_{-1} (M) + k_2],$$

where (M) is the concentration of M. Thus k decreases as (M) decreases, which is the characteristic low-pressure fall-off of the rate coefficient.

This scheme accounted qualitatively for what was ob

[9] The paper was received by *the Journal of the American Chemical Society* in January 1927 so the work was probably done mainly during the latter half of 1926.

served in experiment but not quantitatively: experimentally, 1/k does not vary linearly with 1/(M). Rice recognized that a proper theory would have to be more explicit about the meaning of A* and k_2. He envisaged the complex molecule A as a collection of coupled oscillators and the activated molecules A* as all those that had a great enough total energy to react. However, it was only if that energy were correctly apportioned—particularly, only if some required minimum amount of it found its way into a crucial one of the molecule's vibrational degrees of freedom—that reaction would occur. Rice saw the mean time that had to elapse between the initial energization of A and the favorable reapportionment of that energy as what the primitive versions of the theory had been trying to express as the time lag to reaction, $1/k_2$. He could now, however, relate that time explicitly to the complexity of the molecule: the greater the number of active vibrational degrees of freedom, the longer would it take for the required energy to find its way into a particular one of them. The result was not only a theory in better accord with experiment than its predecessors, but a much more detailed and revealing picture of the dynamics of polyatomic molecules. It is a picture that continues to excite the imagination of scientists. The issues raised by it—central to the study of regular versus stochastic behavior of complex mechanical systems—are the object of much current research.

When Rice left Berkeley and went to Caltech as a National Research Fellow, one of his first concerns (1928b) was to rephrase the unimolecular reaction-rate theory, where necessary, in the language of the (older, pre-wave-mechanical) quantum theory. At Caltech he met Louis S. Kassel, who was working on the same problem along similar lines. (In his 1928 paper, Rice expressed his indebtedness to Kassel for discussions of the problem.) Their names were soon to be linked permanently, when the theory came to be known to all chem ists first as the RRK (Rice-Ramsperger-Kassel) theory, then later as the RRKM theory (after later work with [1951a] and by[10] R. A. Marcus).

It was also at Caltech that Rice did his first landmark work on predissociation and diffuse spectra (1929a,b). The phenomenon of predissociation has much in common with that of unimolecular decomposition, and Rice elucidated the connection. Some of this work was apparently done during a temporary return to Berkeley (for his 1929 paper, "On the Quantum Mechanics of Chemical Reactions," has a Berkeley byline).

It is clear from the papers of this period that Rice was already mastering and applying the ideas and methods of the new quantum theory originated primarily by German physicists. Since, at that time, the Germans were applying the theory most rapidly and widely, the next major step in his studies—a year at the Institute for Theoretical Physics of the University of Leipzig—was a natural one. While he was there he met and benefitted from discussions with Werner Heisenberg, Michael Polanyi, Eugene Wigner, Felix Bloch, and Hartmut Kallmann.

During his stay in Leipzig, Rice worked on problems of inelastic atomic and molecular collisions (1930a,1931a) and extended his earlier work (1929a,b,e) on predissociation. On his return to the United States, he continued his studies of inelastic collisions at Harvard. Referring to Rice's papers (1931b,c) on that subject, L. Landau, writing in 1932, said that until then only Rice had correctly recognized the fundamental role that the crossing of potential-energy curves played in those processes.[11] Landau remarked that previous work had implied a strange disappearance of energy. In an

[10] R. A. *Marcus, Journal of Chemical Physics* 20(1952):359.
[11] L. Landau, *Physikalische Zeitschrift der Sowjetunion* 1(1932):88.

other direction, Rice's method for treating problems in which the collision partners approach slowly but interact strongly (1931e) anticipated what later came to be called the "method of perturbed stationary states."[12]

Recent evaluations have also recognized the perceptiveness of Rice's pioneering work on predissociation (1929a,b,e, 1930c).[13] Wilse Robinson, referring to Rice's work of this period, noted: "Many persons, myself included, working on radiationless transitions in large molecules 30 years later unfortunately were not fully aware, even though we should have been, of the beautiful physical insight into this problem already recorded, dust-covered and forgotten, in the library. Who would guess that one of the best intuitive descriptions of the process whereby a discrete state 'prepared by the absorption of light' interacts with a continuum is contained in that great paper of September 10, 1929 . . . ?"[14]

In collaboration with Harold Gershinowitz at Harvard, Rice also made an early contribution toward the now famous transition-state theory of chemical reactions (1934c). In addition, he mastered the new ideas of valency and molecular structure that arose from the quantum theory. His course in advanced inorganic chemistry at Harvard must have been one of the first in the country to give a systematic presentation of those ideas for young students; now such courses are standard in the chemistry curriculum. Rice's influential book, *Electronic Structure and Chemical Binding* (1940a), which was based on his Harvard lectures, has come to be regarded as a highly original contribution to the pedagogy of chemistry.

After moving to Chapel Hill, Rice continued to pursue his

[12] N. F. Mott and H. S. W. Massey, *The Theory of Atomic Collisions* , 2d ed. (Oxford, 1949), pp. 153-57.

[13] R. A. Harris, *Journal of Chemical Physics* 39(1963):978; G. W. Robinson, in *Excited States*, vol. 1, ed. E. C. Lim (New York: Academic Press, 1974), p. 1.

[14] G. W. Robinson, in *Excited States*, p. 1.

interests in chemical reaction kinetics (both its theoretical and experimental aspects) with vigor. In the early 1960s, he again took up the problem of the kinetics and mechanism of atomic recombination (and its inverse, diatomic dissociation), to which he had been giving intermittent attention since 1941. He presented arguments of great subtlety and generality (1961b) to clarify the question of equality between the equilibrium constant in a reaction and the ratio of forward and reverse rate constants (the "rate-quotient law"). These can be best appreciated in a simple example. In the kinetic scheme

$$A \underset{k_6}{\overset{k_1}{\rightleftharpoons}} A^* \underset{k_5}{\overset{k_2}{\rightleftharpoons}} B^* \underset{k_4}{\overset{k_3}{\rightleftharpoons}} B,$$

with A* and B* being transient high-energy intermediates, the concentrations of which can be treated in steady-state approximation, the rate constants k_f and k_r for the forward and reverse reactions A → B and B → A are:

$$k_f = k_1k_2k_3/(k_3k_6 + k_5k_6 + k_2k_3)$$
$$k_r = k_4k_5k_6/(k_3k_6 + k_5k_6 + k_2k_3).$$

The "equilibrium" approximations to these rate constants (obtained for the forward reaction as k_2 times the ratio of the concentrations of A* and A at equilibrium, and analogously for the reverse reaction) are $k_f^{eq} = k_1k_2/k_6$ and $k_r^{eq} = k_5k_4/k_3$. These exceed the true (i.e., the steady-state) rate constants by the common factor $1 + k_5/k_3 + k_2/k_6$. Thus, although the true rate constants k_f and k_r are less than they are estimated to be by the equilibrium approximation, they deviate from the latter by identical factors, so that k_f/k_r, like k_f^{eq}/k_r^{eq}, is just $k_1k_2k_3/k_4k_5k_6$, which is the equilibrium constant for the reaction $A \rightleftharpoons B$.

This illustrates what Rice found to be a general phenom enon (not only in steady-state approximation): that the ratio kf/kr of the rate constants in a chemical reaction remains equal to the equilibrium constant of the reaction even though k_f and k_r separately are less (sometimes *much* less) than what one would have estimated for them from the equilibrium approximation. Our understanding of the very meaning of a rate constant is now much deeper than it was before Rice's analysis.

Impressive as were Rice's accomplishments in quantum collision theory, energy exchange, and chemical kinetics, they were nevertheless matched in depth and originality by his work on phase transitions and critical phenomena, the dominant interest of his later years. Some of the roots of the scaling and homogeneity principles—which have been important heuristic ideas for understanding the relations connecting thermodynamic singularities at a critical point—are to be found in Rice's studies of the thermodynamics of critical-point and lambda-point phenomena.

He showed (1955b) that when a pure liquid and its vapor are in equilibrium, the isothermal compressibility K of one of those phases at any point T,V on the temperature-volume coexistence curve; the discontinuity ΔC_v that the constant-volume heat capacity undergoes when the coexistence curve is crossed at that point from the one- to the two-phase region; and the rate dV/dT at which the volume varies with the temperature along the coexistence curve at that point, are related by

$$KV\,\Delta C_v = T(dV/dT)^2.$$

If we suppose that as T,V approaches the critical point at T_c,V_c the discontinuity ΔC_v diverges proportionally to a negative power, $(T_c-T)^{-\alpha}$, of the temperature difference

T_c - T; that K diverges proportionally to another negative power, $(T_c - T)^{-\gamma}$; and that V - V_c on the coexistence curve vanishes proportionally to $(T_c-T)^{\beta}$; then we conclude from Rice's relation that the critical-point exponents α, β, and γ are related by α + 2β + γ = 2. This exact relation underlies the slightly more conjectural one (called a "scaling law") that is in common use in present day critical-point theory, in which β and γ are as above while α is the exponent characterizing the divergence of the heat capacity C_v itself rather than that of the discontinuity ΔC_v. If, along the same lines, the pressure p on the critical isotherm deviates from the critical pressure p_c proportionally to a power $|V - V_c|^{\delta}$ of the distance $|V - V_c|$ from the critical point, then Rice may be seen to have discovered, in that same paper (1955b), the special case γ = 1 of a second scaling law, δ = 1 + γ/β. (Four years later, M. E. Fisher[15] reported finding that γ = 7/4 in the two-dimensional Ising or lattice-gas model. Until then, however, it was universally believed that y is always 1, as it is in any of the classical equations of state, explaining Rice's implicit assumption in 1955 that it was 1.)

Rice was also the first to point out that what might have been a lambda transition in a lattice had the lattice been incompressible, might actually, in a compressible lattice, prove to be a first-order phase transition (1954d). This idea gave rise to a substantial body of literature—first, Cyril Domb,[16] following Rice, then many others—and was also confirmed by experiment.[17] Rice's address, "Secondary Variables in Critical Phenomena," delivered in 1970 when he received the American Chemical Society's Peter Debye Award in Physical Chemistry, was an extension of that same theme (1972a). Rice used his ideas about secondary variables to analyze the

[15] M. E. Fisher, *Physica* 25(1959):521.
[16] C. Domb, *Journal of Chemical Physics* 25(1956):783.
[17] C. W. Garland and R. Renard, *Journal of Chemical Physics* 44(1966): 130.

lambda transition in liquid helium (1971a), and also the phase transitions in liquid solutions of the two helium isotopes, ^{3}He and ^{4}He (1967d, 1972b, 1973a), thus contributing to the understanding of what, following Griffiths,[18] is now called a tricritical point. Rice's interest in quantum fluids was of long standing; he had collaborated with Fritz London (1948b), a great pioneer in the subject of superfluidity (as, earlier, in the theories of chemical bonding and intermolecular forces). Both spiritually and geographically, Rice was close to London, for London was at Duke University in Durham, easy commuting distance from Chapel Hill.

Rice was one of the first to treat seriously the fundamental problem of determining intermolecular forces from bulk, macroscopic properties (1941b). His program was continued by Guggenheim and McGlashan,[19] Barker,[20] and others, and has culminated in the accurate rare-gas potentials that are now available. Rice was also among the first to recognize the relevance of the gas of hard spheres to the problem of the structure of simple liquids (1944a); and his was among the pioneering studies of the equation of state of such a hard-sphere fluid (1942d), long predating the accurate determination of that equation of state by computer simulation.

Oscar Rice's experimental studies of critical consolute points in liquid mixtures, including his careful determinations of the shapes of the two-phase coexistence curves, were fully as important for the development of our understanding of critical phenomena as were his theoretical ideas. His aim in making those measurements was to test some controversial ideas then current about condensation and critical points.

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[18] R. B. Griffiths, *Physical Review Letters* 24(1970):715.

[19] E. A. Guggenheim and M. L. McGlashan, *Proceedings of the Royal Society of London, Series A: Mathematical and Physical Sciences* 255(1960):456.

[20] J. A. Barker, in *Rare Gas Solids*, vol. 1, ed. M. L. Klein and J. A. Venables (New York: Academic Press, 1976).

During the 1940s there was much talk of the "derby hat" region[21] near a critical point. Rice did not accept the whole of that picture but was led independently, by his own arguments (1947b), to accept one aspect of it—a flat-topped coexistence curve—as plausible. From Guggenheim's influential paper[22] on the law of corresponding states, which appeared in 1945, it was widely known that as the temperature T approaches the critical temperature Tc, the difference in the densities of a pure liquid and its equilibrium vapor vanishes proportionally to $(T_c - T)^\beta$ (vid. sup.), with $\beta \cong 1/3$. Rice thought that this law might break down just before T reached T_c and that the two phases might still be distinct—in particular, have different densities—when the meniscus between them disappeared; that is, that the coexistence curve would be flat-topped rather than rounded.

Rice gave several particularly illuminating accounts of his and Mayer's ideas: in the paper he presented at a 1948 American Chemical Society symposium on solutions (1949a); the next year in an invited address at the ACS symposium on critical phenomena (1950h); and in his masterly review of critical phenomena (1955j) prepared for Rossini's *Thermodynamics and Physics of Matter*.[23] He pointed out that the same issues arise at the consolute point of a liquid mixture. In the second of the reviews noted above, he reported preliminary results on the coexistence curve for aniline-cyclohexane, the beginning of his famous series of studies on this system (1951c, 1952a, 1953d, 1954b, 1959a, 1960b), some of which have not been surpassed in care and precision to this day. Although he never definitively established the flat top—it is

[21] The term came from a famous diagram that Harrison and Mayer published in 1938 in *the Journal of Chemical Physics*, a figure that bore a fancied resemblance to a hat.

[22] E. A. Guggenheim, *Journal of Chemical Physics* 13(1945):253.

[23] F. D. Rossini, ed., *Thermodynamics and Physics of Matter*, vol. 1 of *High Speed Aerodynamics and Jet Propulsion* (Princeton: Princeton University Press, 1955).

now believed that if there is a flattening it is due only to gravity—his measurements were among the most important in establishing the universality of the critical phenomenon, particularly the underlying identity between the liquid-vapor critical point in a pure fluid and the liquid-liquid consolute point in a mixture.

Among the measurements in Rice's aniline-cyclohexane series was that of the interfacial tension and the rate at which it vanishes as the consolute point is approached (1953d). That was the first such measurement (and is still among the very few) to determine the critical-point exponent for surface tension at a liquid-liquid consolute point. To within experimental error the exponent is identical with that at a liquid-vapor critical point, further confirming the essential identity of those two kinds of critical point. Rice had long recognized the central role of surface tension in critical phenomena; indeed, it had played a prominent part in his earlier theory (1947b). To the end of his life he continued to return to the problems of the structure and tension of interfaces. For him it was the closing of a circle: Some of his earliest papers, dating from his student days at Berkeley and published between 1926 and 1928, were on that theme, as were his last six papers, published between 1976 and (posthumously) 1979.

Rice's *Electronic Structure and Chemical Binding*, to which we have already referred, was his first full-length book. More than a quarter of a century—and a hundred research papers—later, he wrote his second, *Statistical Mechanics, Thermodynamics, and Kinetics* (1967a). There is hardly a topic in it to which he himself had not made a major contribution. It is a particularly original text.

We have had occasion above to mention some of the honors that came to Oscar Rice, including the ACS Award in Pure Chemistry and the ACS Peter Debye Award. There were others. He was given the Southern Chemist Award in 1961; the North Carolina Award in Science, presented by the governor, in 1966; the award of the American Chemical Society's Florida section in 1967; and the Charles H. Stone Award of the ACS's Carolina Piedmont section in 1972. He was elected to serve successively as secretary-treasurer, vice-chairman, and chairman of the Division of Physical and Inorganic Chemistry of the ACS from 1942 to 1944, and he was elected chairman of the ACS's North Carolina section for 1946. He was twice an associate editor of *the Journal of Chemical Physics*, first from 1934 to 1936, starting with the second volume of the *Journal*, and again just after the war, from 1945 to 1947. He was named a fellow of the American Physical Society and a member of the Board of Sponsors of the Federation of American Scientists. He served on the National Science Foundation's Advisory Panel on Chemistry (1958-1961), on the North Carolina Governor's Scientific Advisory Committee (1961-1964), and on the chemistry panel of the Army Research Office, in nearby Durham (1967-1972). He was elected to the National Academy of Sciences in 1964.

About every great man legends grow, often reflecting quirks of habit or personality. Oscar Rice was famous for apparently sleeping through seminars and then asking perceptive and penetrating questions of the speakers. He was notorious for the clutter of his office, piled high with books and papers in seemingly random array—which did not keep him from laying his hands instantly on whatever was sought. Then there was the famous armchair, which, as we saw, even made its mark on the Oak Ridge establishment.

In manner Rice was quiet, gentle, and modest, but never hid his enthusiasm for science, which was obvious to all. His writings show how great was his strength—the firmness of his grip on his subject and the clarity and certainty of his vision. But even his published papers, powerful and compel ling as they are, have a calmness and restraint that reflect the reasoned judgment of their author.

The careers of Oscar Rice and the late Henry Eyring (1901-1981) ran closely parallel. They were nearly the same age (Eyring was two years older); they were contemporaries as graduate students in the Berkeley chemistry department; they both witnessed the development of quantum and statistical mechanics and applied them widely through physical chemistry; and they shared abiding interests in problems of chemical kinetics, liquid structure, and phase transitions. Although their public styles could hardly have been more different, their personal habits were much alike: "Henry . . . was abstemious to the extreme, no coffee, no tea, no alcohol, no very hot or very cold foods. Commenting on this Oscar said that the only difference between him and Henry was that he ate coffee ice cream."[24] On hearing that remark, anyone who knew Oscar would have recognized its tone. His humor was never caustic but was as gentle as his manner, yet it was sudden and spontaneous. His quips were always accompanied by a smile and a sparkle that are still recalled by friends and family.

Rice's counsel was sought and valued by his students and associates. He gave them generous help at the start of their careers and loyal support thereafter. He was a selfless and devoted teacher, more interested, we recall from personal experience, in the development of his coworkers than in his own aggrandizement. In our regular individual meetings with him to discuss papers in the literature, he was always careful to point out the tacit assumptions the papers made and that we might have missed. Those were valuable lessons.

By all who knew him Oscar Rice was loved as a friend, held in the highest esteem for his accomplishments as a scien

[24] Letter of October 18, 1982, by H. Gershinowitz to the authors.

tist, and admired for his courage. He withstood years of painful illness without complaint and with thought only for the welfare of others. He fought injustice and intolerance wherever he saw it, without thought to the popularity of his cause. When none would speak out with him, he spoke out alone.

> He is remembered for his concern for the rights and freedoms of people everywhere, for his tolerance, for his patience with persons with whom he disagreed, for his unwillingness to be reconciled to injustice . . . [He] championed scholars who were denied academic freedom, he worked for the elimination of racial segregation, he defended the rights of all citizens to freedom of expression and action in the redress of grievances.[25]

In the following statement of regard for his university, Rice speaks eloquently of his concern for human rights: "I should acknowledge my indebtedness to the University of North Carolina, which for the past 25 years has provided good working conditions, an interesting and stimulating teaching program, and a situation both pleasant and conducive to research. I value not only these aspects of my life at this University, but also the atmosphere of free and open discussion which I have found there, the acceptance of new ideas, and the growth of a new cosmopolitanism, which now encompasses not only people of the far corners of the world, but also some Americans who until recently have been partially excluded from the world of culture through irrelevant circumstances, not connected with their own worth and value."[26] Oscar Rice served his fellow man as he served his science—with courage and distinction.

[25] From a memorial resolution proposed by Rice's colleagues and adopted by the faculty of the University of North Carolina at its meeting of September 15, 1978.

[26] O. K. Rice, on receiving the Southern Chemist Award of the Memphis section of the American Chemical Society, in New Orleans, 1961; quoted in the August 28, 1981 edition of the *University Gazette* (University of North Carolina, Chapel Hill), in an article about the establishment of the Oscar K. Rice Lectureship in the Department of Chemistry.

The authors of this biography were postdoctoral associates of Oscar Rice: R. A. Marcus from 1949 to 1951 and B. Widom from 1952 to 1954. For helpful correspondence and conversations about Oscar Rice we are grateful above all to his wife, Hope Sherfy Rice, and to A. O. Allen, M. Burton, E. L. Eliel, W. Forst, H. Gershinowitz, F. Kohler, J. C. Morrow, and R. G. Parr.

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Conway Studios Corp., New York, New York

Dickinson Woodruff Richards

October 30, 1895-February 23, 1973

By André Cournand

It is only when Death builds its frame around life that the portrait of a man is really hung on a wall.

—*HENRY JAMES*

True friends create the charm of life, their passing, its bitterness.

—*ANONYMOUS*

Modesty and greatness seldom harmonize in one individual. Dickinson Woodruff Richards ("Dick"), to whose memory this biographical sketch is dedicated, is one of those few in whom these apparently opposite qualities balanced one another.[1] Although modest to the point of shyness, he implemented his natural intellectual gifts through strong character and hard work, reaching the heights in whatever he undertook—whether as a schoolboy, college and medical student, physiologist, medical scientist, clinician, chairman of a teaching service in a municipal hospital, organizer of two research laboratories in the field of cardiopulmonary physio

[1] The following account of my friend's life and works is derived from several briefer ones I published after his death at the request of societies to which he belonged. It first appeared in my autobiography, *From Roots . . . to Late Budding* (New York: Gardner Press, Inc., 1986), pp. 165-182.

pathology at the College of Physicians and Surgeons of Columbia University, medical consultant to a leading pharmaceutical firm, adviser to the Committee of Medical Research (CMR) of the Office of Scientific Research and Development (OSRD), educator, historian, reformer, or humanist.

This essay by his friend and close collaborator for more than forty years will evoke Dick's life and his fundamental contributions in these many and diverse situations in an attempt to recreate, ten years after his death, the image of a man who achieved greatness by exacting perfection of himself in whatever activity he was engaged.

A retrospective overview of a man's life may lack objectivity when attempted shortly after his death, feeling then prevailing over critical and well-documented judgment. In this last of many tributes to my friend, the essential features of his character and accomplishments will be derived from my personal recollections, from information tendered by members of his family, and by a number of his colleagues and students. Dick's correspondence, and his published and unpublished writings, will also contribute.

FAMILY BACKGROUND: CHILDHOOD, SCHOOL, AND COLLEGE EDUCATION; MEDICAL AND PHYSIOLOGICAL TRAINING (1895-1928)

Dickinson W. Richards was born October 30, 1895, in Orange, New Jersey. His ancestors on both sides had settled in New England (Massachusetts and Connecticut) during the seventeenth century. His paternal grandfather was a Congregational minister, as was one of his uncles, and his father was a lawyer. On his maternal side, among the Lamberts, physicians prevailed. His grandfather practiced general medicine in New York City after medical training at Bellevue, then the city's largest municipal hospital. His three uncles achieved leading positions in the medical profession. All three were connected either with Bellevue Hospital or the College of Physicians and Surgeons, or both.

Dick himself has this to say about the opposite traits of character to be found in both lines of forebears, all of whom were New Englanders sharing a common tradition. On his father's side he saw them as "believers; conformist; noncurious; judicious, steady, firm; noninnovators; meditative, nonscholarly" and on his mother's side, "nonbelievers, nonconformists; curious; vigorous, quick-tempered; innovators, crusaders; scholarly, nonmeditative." The harmonious selection among both sets of traits was evident in Dick's own character and behavior.

Already in his early life are found traces of the distinctive aspects of his personality: innate shyness and modesty, an enormous capacity for work, and the natural bent of a scholar. Dick's modesty did not interfere with the development of his aptitude for learning. A picture of the schoolboy and student at the Hotchkiss School in Lakeville, Connecticut—where, following a family tradition, he received a classical education in the humanities: English, Greek, and history—is drawn from the testimony of a classmate, William Albert Olsen, who later became his brother-in-law: "At commencement, it became automatic that Dick would be called to the platform to receive handsome books for being first in every course he took. He literally walked off with an armful of prizes!" On the wall of the study hall still remains the inscription: *Dickinson Richards, Jr., 1913. Total Year Average: 93.4*.

When he entered Yale University as an undergraduate, he was following a tradition upheld by all the young men among his forebears, whether Richardses or Lamberts. According to Bert Olsen, "He won the Hugh Chamberlain prize for Greek entrance examinations with the highest mark ever obtained." Dick used to communicate in ancient Greek with his room mate Bellinger (who later became a professor of Greek at Yale), discussing in this language everyday problems arising in college. Professor Bellinger, recalling his friendship with Dick, stated that, "when evaluating any [other] man, he always used the scale of D.W.R., set at 100."

While at Yale, in addition to pursuing his studies in the humanities, Dick acquired a good background knowledge of mathematics and natural sciences, and, as Olsen reported, "led his entire class in grades throughout his undergraduate years." Yet these scholastic achievements did not deter him from finding time for extracurricular or athletic activities. At both institutions he was editor in chief of the school journal. At Hotchkiss he received his letter in high jumping; at Yale he shifted to rowing, but was unsuccessful in his attempt to make the varsity squad.

After graduation in 1917, Dick joined the army and, in 1918, near the end of World War I, crossed the Atlantic with an artillery unit in which he served as lieutenant. Upon his return from Europe and discharge from the service in 1919, the time came for Dick to decide on a career. His choice was the medical profession—not surprising, given a grandfather and three uncles who had responded to similar calls! Dick entered the College of Physicians and Surgeons in 1919. Owing to his enormous zest for work, he not only completed his medical studies brilliantly, obtaining his M.D. in 1923, but also his master's degree in physiology at the end of his third year under the guidance of Professor Ernest L. Scott. Forty-three years later, in 1966, Dick paid his debt of gratitude to his first teacher of physiology by bringing to light documents, totally ignored until then, upon which Scott's Ph.D. thesis had been based: The data collected back in 1911 clearly demonstrated the favorable effect of a pancreatic extract, which he had prepared, upon depancreatized dogs.

After graduation he continued his training in medicine as an intern and as a resident in medicine at the old Presbyterian Hospital from 1923 to 1927. During this period he formed close friendships, which proved to be lifelong, with Robert Loeb and Dana Atchley. Both were members of the staff of Presbyterian Hospital, newly affiliated with the College of Physicians and Surgeons. Both of these gifted friends guided Dick's earliest footsteps in hospital practice and clinical investigation.

However, the men who most affected his mind and actions in these years were, by his own account, two outstanding physiologists from whom he derived his grounding in physiological research and his approach to scientific medicine and clinical investigation, which would shortly rival the basic knowledge acquired earlier in the century. Of their early influences, Dick said: "A man's mind and his actions are chiefly molded by a very few. For me, in the early years, these were Lawrence J. Henderson and Henry Hallet Dale."

Although Dick never worked in the Fatigue Laboratory, created at the Harvard Business School by L. J. Henderson, the professor's influence on and interest in the budding physiologist were strengthened by numerous exchanges of letters and by Dick's frequent visits to Cambridge, Massachusetts. These exchanges had been facilitated by Dick's Yale classmate and friend Cecil Murray. It was from Henderson that Dick derived what was to be the guiding idea of his work in human physiology and physiopathology. To his influence must be traced one of Dick's earliest publications (in 1927), "The Oxyhemoglobin Dissociation Curves [curves defining the affinity of hemoglobin for oxygen at various pressures] of Whole Blood in Anemia," which supplied the first experimental evidence of a disease-induced decrease in the affinity of hemoglobin for oxygen in man.

Under Henderson's tutelage Dick published three papers during his residency: one on the circulatory adjustments in anemia; another on the blood flow through the lung and systemic circulations, quantitatively defined (for the first time) in a patient with tetralogy of Fallot; and a third one on the influence of posture upon the mechanics of blood flow.

On several occasions Dick Richards paid tribute to Professor Henderson as his mentor in physiology and his ideal as a scientist. The most notable of these was Dick's speech at the respiration dinner of the American Physiological Society held during its meeting in Chicago, in April 1957. Here, Dick offered the following portrait:

> It seemed to me he was quite a bit like Socrates, the Socrates of those early dialogues when he was young and lively, poking fun at aged philosophers and straining the wits of young ones . . . It may as well be said now as later that in spite of his complete freedom of mind, in personal demeanor Henderson was always most courteous and considerate. That Jeffersonian phrase, "a decent respect for the opinions of mankind" applied well to his manner of life. . . .

Dick's description of what it was like to discuss actual work in progress with Henderson vividly depicts their personal relationship at this early time:

> What would happen was something like this. You would work and strive to put your experimental ideas together, then go to the Professor and tell him about them. He would then either decapitate your entire brainchild in a single whistling sentence, or else take about three more sentences to put your ideas in order for you, and you would come back and start to work. Then (after a while) you would go back again with what you had done, and again, with great kindness, yet with still the same unsparing critique, he would take your work apart. If there was anything left, after he finished with it, you would feel elated and go back and try some more.

At the end of his residency, Columbia University awarded Dick a research fellowship to work at the National Institute for Medical Research in London, England, during the period 1927 to 1928. There he worked under the guidance of Henry

Dale. Looking back on this period of training in experimental physiology, Dick had this to say about his British mentor:

> [Sir] Henry Dale could theorize, too, but his [mind] was [as compared with that of L. J. Henderson] different. Dale was primarily an experimenter and continued this through almost all his active years. . . . On a day when an experiment was planned, Collison, the head technician, would start at some time in the dark British predawn; Walter [Bauer][2] and I would arrive about nine . . . we were working on the dog's hepatic circulation. Just as we reached the key point of cannulating the blood vessels and bile duct, the laboratory door would fling open, and Sir Henry (Dr. Dale as was then) would come charging in, often in morning coat and striped trousers, grab a lab coat off the hook, and be with us in seconds. What is more, he would stay until the experiment was finished, whether at tea time, dinner time, or later.
>
> As it happened, it was in the spring of 1928 that the concept of the chemical transmission of the nervous impulse was born. Our job in this was the simplest, to test in cats the vasodilator principle—supposedly histamine—in extracts of horses' spleen. I recall one afternoon when the testing was finished, I had some extract left over, and I went on to acidify and then alkalinize samples of it and test them again, to find, suprisingly, that on the alkaline side of neutrality all vasodilator activity disappeared. This would not occur with histamine, but would with acetylcholine. I reported this to Dr. Dale at tea that day, and he said, "Hmm," no more. But this was clearly one small addition to many things he had been thinking about, because only a few days later he began to construct for us the possibilities of acetylcholine as a biological agent. The generation of a great idea in a first-class research mind, over months and years, is a remarkable thing.

One can only admire the way Dick modestly neglects to emphasize his own role, a trait that was so significant throughout his entire scientific life. In any case his work in Henry Dale's laboratory was sanctioned by the publication in the *Journal of Physiology* of two papers, one in collaboration with Walter Bauer on the vasodilator effect of acetates, and

[2] Bauer was another American research fellow with whom Dick maintained a lifelong friendship.

the second in collaboration with Walter Bauer and Henry Dale on the control of the circulation in the liver.

More significant for his career as an investigator, Dick's training in Dale's laboratory was to prove of particular value in later years when he familiarized himself with the technique of right-heart catheterization in experiments on dogs and in a chimpanzee.

At the end of the tenure of his research fellowship, Dick Richards returned to New York. In 1928 to 1929 he began his career as a clinician, teacher, and independent clinical investigator, pursued entirely at the Columbia-Presbyterian Medical Center and at the Columbia University Division of Bellevue Hospital until his official retirement.

EARLY CLINICAL INVESTIGATIONS (1928-1932)

Upon his return from London in the fall of 1928, Dick was to join the other members of the Department of Medicine in the newly created Columbia University-Presbyterian Hospital Medical Center as an assistant in medicine and assistant physician. The members of the department, under the chairmanship of Walter Palmer, included one of the most brilliant groups of fulltime investigators, clinicians, and teachers in North America.

Dick turned to the problem of how to equilibrate O_2 and CO_2 in a lung-bag system in order to estimate their concentration in the mixed venous blood. A first application of the method, known as "indirect Fick," was to study the effect of therapeutic pneumothorax upon the pulmonary blood flow. It so happened that this investigation was to play an important role in Dick's personal life as well. A young graduate of Wellesley College, Constance Riley, came to work in Dick's lab as a technician. They became engaged in 1930 and married in September 1931.

A survey of Dick's scientific activity after his return from

London is not limited to the research already mentioned. In 1929, in collaboration with Alvin Barach (a part-time member of the Presbyterian Hospital clinical staff), he initiated a series of investigations, pursued during the next five years. The studies concerned the effects of oxygen therapy in chronic cardiac and pulmonary diseases, including cardiac failure, pulmonary tuberculosis, pulmonary fibrosis, and emphysema. Dick was well prepared for these studies since they had as their particular focus of interest the effects of oxygen therapy on serial blood respiratory gas and electrolyte responses. For the first time, they observed the seemingly paradoxical response to O_2 therapy in certain pulmonary diseases (fibrosis and emphysema) of a high CO_2 tension that developed as a result of the relief of hypoxia followed by reduced ventilation.

THIRTY YEARS OF COLLABORATION WITH A. COURNAND (1932-1961)

To Dick himself should be left the occasion to present, in his own terms, how he envisioned the long period of his collaboration with me. This purpose will be served by reference to the contents of a letter he wrote in December 1972, to Julius Comroe, a distinguished colleague who since the mid-1940s had greatly contributed to pulmonary physiology and physiopathology. In this letter Dick established the natural sequence of his investigative work. The first sequence, termed by Dick "Blood and Circulation," deals with the investigations mentioned previously during the period 1922 to 1932. The second sequence is the signal of his extending interest from "Blood to Lung" in order to cope with "neglect of lung performance by cardiocirculatory physiologists." This latter period stretched from 1932 to 1942. A series of tests and the equipment these necessitated were devised for the analysis of the various components of the pulmonary func tions as they were observed in normal subjects in whom standard measurements were established and in patients with various forms of chronic pulmonary diseases.

The beginning of the third sequence, from 1940 to 1961, termed by Dick "Lungs, Blood, and Circulation," is heralded by the introduction into clinical investigation of the technique of cardiac catheterization. This additional technique enabled the exploration of the dynamics of the cardiac functions—output, filling and ejection pressure, pulmonary and systemic blood flow. In association with implementation of the techniques established during the previous periods, the new technique heralded the crowning fulfillment of the plan laid down for him by his mentor, L. J. Henderson, allowing the description of the successive phases of respiratory gas transport from the atmosphere to the tissues in normal humans as well as in an almost limitless variety of diseases.

Our daily collaboration over several decades provided a unique opportunity for observation and insight. To begin with, my recollections, vivid in my mind, are of his display of technical skill—he was truly ambidextrous—and efficiency; of his care and caution in studying human subjects; of his implementation of self-experiment in the true tradition of the British and Scandinavian respiratory physiologists; of his foresight and careful planning, which included taking advantage of the unexpected and stressed methodological innovations; and of his thorough knowledge of medical literature, current and classical.

For all his affability, even temper, and friendliness, Dick was a hard taskmaster and a demanding teacher, always probing the prior question, exacting high accuracy in the collection of data and strict objectivity in their interpretation. He expected from his associates, if not the perfection, then at least the work pace that he set for himself. Indeed I recall my mixed feelings when confronted by a deluge of books, manuscripts, and reprints fed to me in our early meetings and during my initiation into the many techniques I was supposed rapidly to master.

Dick Richards's contributions to medical research were not limited to physiology and physiopathology. In 1934, without any letup in his other activities, he became medical advisor to Merck's research organizations. His expanding knowledge of medical science and medical affairs was a great asset in formulating therapeutic research policies. These policies were particularly fruitful during World War II, as they led to close cooperation among scientists in government, industry, and the universities. They also led to a valuable reduction in the time lag between discovery, clinical testing, and practical use of such agents as drugs, antibiotics, and vitamins.

At the end of the war, in 1945, he became the head of Columbia University's First Medical Division at Bellevue Hospital; at the same time he was promoted to the fulltime Lambert Professorship of Medicine at the College of Physicians and Surgeons. In these functions he gave his full measure as a leader in clinical medicine. One of his former residents, Thomas Q. Morris, recalls him as a teacher of physicians in these terms:

> Members of the Bellevue Hospital House Staff who made rounds with Dr. Richards saw him as a multifaceted man—clinician, teacher-scientist, and chief-of-service. His impact on physicians in training can be fully appreciated only in his meld of these three roles. As a gentle clinician—concerned in the utmost for the comfort of his patient, but, above all, the master of clinical judgment—able to discern the proper course in a labyrinth of clinical and laboratory data though never reluctant to seek consultative advice. As a teacher-scientist—applying principles and results of research to interpretation of clinical phenomena and toward improved medical treatment, and awakening investigative potential in residents and interns through his attitude of constant inquiry. And finally as chief-of-service—always available to members of his house staff, fostering an at

> mosphere conducive to the happy blend of excellent patient care and fruitful clinical investigation, and willing (and able) to do combat with the administrative structure of a municipal hospital system.

Indeed, as a member of the Bellevue Medical Board, Dick was outspoken and unyielding in his criticism of the city's neglect of its hospitals and in his efforts to bring to bear pressure to oblige the city to erect a new hospital building. On the occasion of his retirement in 1961, he received, as a commemorative gift from his colleagues, a bronze replica of the casting surrounding the elevator call buttons in the ancient (dilapidated) A and B Buildings of Bellevue.

Dick's retirement was, of course, anything but that. Around that time, with Alfred Fishman's help, he was deeply engaged in the planning and editing of the book *Circulation of the Blood: Men and Ideas*. An unrelentingly critical, albeit sympathetic, editor Dick was perhaps the most severe judge of his own thought and expression.

His last ten years, without letup, were devoted to multiple scholarly undertakings and to a quest for a more decent world and a safer environment.

To the medical historian we owe a deep and illuminating knowledge of his two medical heroes, Harvey, the scientist, and Hippocrates, the practicing physician and natural philosopher; and the creation and implementation of a program of teaching in biomedical history that emphasizes men and ideas rather than facts and chronology.

One of D.W.R.'s most notable achievements was to discover what his hero, Hippocrates of Cos, looked like and who he was. This search for an authentic portrait of Hippocrates and his interpretation of the famous First Aphorism, "Life is short, art is long, opportunity fleeting, experiment treacherous, judgment difficult," are landmarks in the field of anthropological detection and testament to his perseverant curiosity and profound knowledge of the Greek language. An article published in the June 17, 1963 issue of *the Journal of the American Medical Association* recounts the story of the discovery and identification of a marble bust of Hippocrates in 1940 near the ruins of Ostia Antica, a seaport of imperial Rome. The word-by-word analysis of the quartet of epigrams forming the first part of the First Aphorism was published in the 1961 issue of *Perspectives in Biology and Medicine*.

Richards, a science philosopher, proposed a system of diseases in which recognizable biologic trends have nonhomeostatic properties: the excessive, the defective, and the inappropriate. He also rejuvenated the Platonic concept of Taraxis, or disorder, which our whole human experience imposes on the interpretation of environmental phenomena and the events of life. He emphasized that the chaos, the senseless, and the suffering lead in medicine to the reestablishment of order.

In many lectures, Richards, the reformer, advocated new methods of medical teaching, stigmatizing the pretension of man to become the Lord of Creation without anticipating the consequences of his ill-used power over nature.

In the humanist we can admire a sense of the human, which is not a mere orientation of the intellect but a profound attitude involving the entire being. In the reformer, we admire the man concerned with the consolidation of the promise of the future and the limitation of its threats.

But life was not only work; it was also relaxation in the country surroundings where Dick brought up his four daughters. Each summer he enjoyed his return to the large and simple house built by his parents on Lake Sunapee in New Hampshire. There, many years ago, a lonely foreigner, sitting at the table over which Dick's mother presided, discovered and enjoyed the comforting and warm spirit of a closely knit American family. In this setting also, roughing it along the trails of the White Mountains, grew and ripened a friendship, of which, on another memorable occasion, I said that "its essence was not to look in each other's eyes, but to look in the same direction."

Late in his retirement, he published a small volume, *Medical Priesthoods and Other Essays*, that contained those of his lectures he believed to be entertaining and to express his general ideas on medicine and the physiology of the heart and lungs, as well as on other topics. In this volume, in line with his dominant intellectual concerns, we hear him commenting on the relegation of a stethoscope to a display case in a university hospital:

> Let us pause for a moment and contemplate this humble little device, the stethoscope, by and for itself. Look at it as it hangs on its hook, with its ears up and its rubber legs twisted.
>
> Has anyone ever commented how remarkably in this posture it simulates the snakes of the caduceus, the symbol of our friend Aesculapius? Well, one can say that in this particular posture it is indeed equally symbolic, and equally useless with the aesculapian wand.
>
> But now suppose we put the thing into operation. There occurs a metamorphosis. . . . This ancient and outdated instrument of nickel, rubber, and plastic has one attribute that transcends all the laboratories that ever were or ever will be built. In order for the stethoscope to function . . . there has to be . . . a sick man at one end of it and a doctor at the other. The doctor has to be within 30 inches of his patient. It won't work by long distance telephone, or by word of mouth through half a dozen intermediaries, or by radio, or by television, or in a dry clinic, or even in a committee. . . . We are concerned over the widening gap between the clinic and the laboratory, the interest in the measurement and the neglect of the person. . . . Be assured that I am in no sense arguing against the physician working in the laboratory. But once a physician does take upon himself the responsibility for a patient's care, he becomes a different man. He accepts a social discipline. He must define the problem anew . . . in each particular case. . . . Human suffering pervades the whole sick man, and this whole must be cared for. Hippocrates said it more clearly . . . than anyone: "It is necessary for the physician to provide not only the needed treatment, but to provide for the sick man himself, and for those beside him, and to provide for his outside affairs."

In *Medical Priesthoods* there also were two of his writings on Hippocrates, long of interest to him and now, according to his preface, his "chief preoccupation." In one of these essays, "Hippocrates and History," he succeeded in weaving into one fabric his dominant intellectual concerns—those of physician, classical scholar, humanist, and social critic.

One facet of Richards—the social critic—I have already mentioned in connection with his effort to provide a better plant at Bellevue. Important as this was, it would not do to leave the matter there, for like his uncle Alexander Lambert, who in the 1920s urged that the medical profession develop what we today would no doubt term new models of health care to better meet the needs of the population at large, Dick was not always content with existing patterns of practice.

To my mind this illustrates one aspect of Dick's extraordinary progression: the child and young man, brought up in a New England tradition, from early on demanding perfection of himself, presenting a rare example of a happy marriage from which issued four daughters and many grandchildren; mastering medicine and contributing substantially to cardiopulmonary physiology; withstanding with easy grace the challenge to personal integrity occasioned by the highest recognition afforded scientists and physicians; remaining the man formed by his early training, education, and culture, and yet going far beyond them, as reflected in one sense in the above statement and in another in his inspired new understanding of Hippocrates.

As I noted at the outset, Dick's modesty remained fundamental throughout his life. When he was awarded the Nobel Prize in Physiology or Medicine in 1956 and the Kober Medal in 1970, he converted each occasion into one for the detailed appreciation of the work of his colleagues and peers. Proffered many doctorates *honoris causa*, he accepted but two: one from his *alma mater* and the other from the univer sity with which he was to be connected for more than fifty years.

In the task of paying a last tribute to my friend, I have been guided by what appeared essential in the man. And yet I have not touched on his enormous correspondence, couched in his fine, precise writing, which he sustained on a multitude of topics with scientists, philosophers, historians, colleagues, former students, and friends. Nor have I listed all the honors, endowed lectureships, editorships, committee memberships, and organizational assignments bestowed upon him. Such an enumeration would not have satisfied his deliberate avoidance of easy effects.

What, then, of the essence of the man? With Alfred North Whitehead and Shmuel Sambursky, Dick affirmed that the "language of Science is incapable of application to, or use in the description of, the qualities of consciousness." To characterize "man's essence—actual" he cited, with his deeply felt pessimism, *Measure for Measure:*

. . . man, proud man,
Drest in a little brief authority,
Most ignorant of what he's most assured,
His glassy essence, like an angry ape,
Plays such fantastic tricks before high heaven
As make the angels weep.

And of "man's essence—ideal" he wrote to me, "Man's potentiality, or in these days his survival, will depend on his consciousness, more specifically his conscience, more specifically still, the ability of the leaders and their followers to change character, into *more merciful beings*." If one believes, as he did, that science is of no use in the description of the transformation of which he writes, those who knew him may yet feel that his character provides an example of what can be accomplished.

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J. F. Chappell

Charles Donald Shane

September 6, 1895-March 19, 1983

By S. Vasilevskis and D. E. Osterbrock

C. Donald Shane was born, grew up, and lived all his life in California. He was well known not only for his research, but, especially for his initiative, leadership, and administration of scientific projects and programs. The most prominent period of Shane's professional life was his directorship of Lick Observatory of the University of California from 1945 until 1958. During those thirteen years, he initiated and virtually completed the 120-inch reflector, the largest Lick telescope. It was named after him in 1978. At Lick Observatory he also carried out his monumental program of counting external galaxies and investigating their distribution.

LIFE HISTORY

Shane was born on the Futhey ranch near Auburn, California, on September 6, 1895, the eldest of four children. According to family tradition, an ancestor on his father's side, James McShane, had come from Ireland about 1745 and settled on Long Island. Soon after his arrival in America he dropped the "Mc" from his name. His son, James Shane, migrated west to Pennsylvania. Later he became one of the early settlers of Ohio. Donald Shane's father, Charles Nelson Shane, was born in Adamsville, Ohio, in 1861 and moved to

California in 1886. He settled in Placer County and was appointed teacher in the one-room Lone Star School, about eight miles north of Auburn.

One of Donald Shane's ancestors on his mother's side, Patrick Futhey, escaped from Scotland after taking the losing side in a "civil war" (or rebellion, as the winning side called it) and settled in Ireland. His son Robert I. Futhey came to America about 1730. Robert I. Futhey's son, also named Robert, was reported to have married Isabella Kidd, daughter of Captain Kidd. The family moved westward step by step, and in 1882 Donald Shane's grandfather, Robert Scott Futhey, made the long trip from Kansas to California, where he established a ranch near Auburn. His daughter Annette taught in various one-room schools in Placer County. In 1894, she married Charles N. Shane while he was principal of Auburn Grammar School. He was elected Superintendent of Schools for Placer County and served in this position from 1902 until 1910.

Donald Shane spent his childhood in a semi-rural environment with plentiful opportunities for outdoor recreation. On graduation from the Auburn Grammar School, he entered Placer County High School, which he attended for two years. His parents, concerned with the education of their children, decided to move to the bigger city of Oakland. Consequently, Charles N. Shane and his son went there in July of 1910, six months before the expiration of the father's term as superintendent. Charles N. Shane obtained a position in the Oakland school system and Donald continued his education at Oakland High School. His mother was appointed to fill out the unexpired superintendent's term in Placer County, and then she also moved to Oakland with the rest of the children in 1911. Donald Shane was fortunate in having very good teachers in Auburn as well as in Oakland. He entered the University of California at Berkeley in 1912.

Shane's interest in astronomy had been awakened at the age of ten by his reading and by conversations with his uncle Edgar Futhey, whose interests were wide-ranging despite his limited formal education. Shane's interest was further stimulated by his teachers in Auburn and Oakland. Still, he was not certain that he could make a living in astronomy. He chose to major in this subject only after the University of California advisors assured him that the Berkeley Astronomy Department was outstanding and that he would have no problem finding a good position in this field. It was indeed one of the best astronomy schools in the United States.

At that time the faculty of the Berkeley Astronomy Department consisted of three members: Armin O. Leuschner, its founder and chairman, R. Tracy Crawford, and Sturla Einarsson. They taught orbit theory, celestial mechanics, observational and spherical astronomy, and general astronomy. In addition, Shane took a number of mathematics and physics courses. By taking a heavy load of courses, carrying out a special project, and attending one summer session, he graduated in 1915, after three years instead of the normal four. He was then appointed a teaching fellow in mathematics for the subsequent year, during which he started his graduate work in astronomy, mathematics, and physics. He held the Lick Observatory Fellowship, with residence on Mount Hamilton, in 1916-1917 and again in 1919-1920. Not accepted for military service in World War I because of a minor medical problem, Shane instead taught navigation in Oregon and Washington for the United States Shipping Board from 1917 until 1919.

Shane received his Ph.D. degree in astronomy in 1920 and was appointed an instructor in mathematics at the University of California at Berkeley. Gradually he transferred his activities into astronomy, becoming assistant professor of astronomy in 1924, working up to professor in 1935, and then chairman of the astronomy department in 1941. During World War II, Shane served from 1942 to 1945 with the Manhattan Project, first as assistant director for scientific personnel of the Radiation Laboratory in Berkeley and subsequently in the same position at Los Alamos, New Mexico. In 1945 he became director of Lick Observatory. He resigned from the directorship in 1958 but remained an astronomer on the active faculty until 1963, when he retired at the age of sixty-seven.

In 1917, Shane married Ethel L. Haskett, who had been the Lick Observatory secretary while he was there. She died in January 1919, two weeks after their son Charles was born. At the end of 1920 Shane married Mary Lea Heger, and their union continued until the end of his life. Their son, William Whitney, was born in 1928.

RESEARCH

Shane started his research as an undergraduate at Berkeley under Leuschner, whose field was orbit theory and celestial mechanics. Shane's first publications were thus concerned with the elements and ephemerides of comets. He considered writing his doctoral thesis on the orbit of the fifth satellite of Jupiter, which had been discovered by E. E. Barnard at Lick Observatory in 1892. This satellite presented some interesting problems in celestial mechanics because of its proximity to the massive, nonspherical planet. However, when Shane went to Mount Hamilton as a Lick Fellow in 1916, his interest turned to astrophysical problems. For a time he entertained the idea of observing stars at the edges of dark nebulae to find out if he could detect reddening of their light resulting from selective absorption. The outstanding theoretical astronomer Henry Norris Russell discouraged him from undertaking this seemingly hopeless task, though in 1930

Robert J. Trumpler at Lick Observatory did discover the reddening that results from interstellar absorption.

Under the influence of Joseph H. Moore and particularly W. W. Campbell, Shane became interested in spectroscopy. Carbon stars had a special attraction for him and he ultimately did his thesis on their spectra. It resulted in two publications that had considerable influence on subsequent research in this field. Because of the superior spectroscopic equipment then available at Lick Observatory, Shane was able to show that what had previously been supposed to be bright emission lines in the spectra of carbon stars were actually gaps between absorption lines and bands.

While working on his thesis Shane also became interested in *o* Ceti, the well-known long-period variable star, and published several papers on its spectrum and on the spectra of novae and other objects. Later he became fascinated by light interference phenomena and applied a Fabry-Perot interferometer to measure the profiles of solar absorption lines. He spent two summers at Mount Wilson Observatory making spectrographic observations of the sun with the Snow telescope and with the 150-foot solar tower. Subsequently, he had a coelostat and a spectrograph built for solar observations at Berkeley. In collaboration with Frank H. Spedding and Norman S. Grace, Shane did some laboratory research in atomic physics involving heavy hydrogen with this spectrograph. Though Shane was bright, clever, and quick to grasp any new idea up to the time his astronomical career was interrupted by World War II, he had not carried out any long-term research programs nor carved out any field as his own. Only after the war did he carry out his monumental program as director of Lick Observatory.

In 1934, Lick astronomer William H. Wright had obtained funds from the Carnegie Corporation for the design and construction of a powerful 20-inch astrograph to put into practice his idea of measuring stellar proper motions with reference to distant galaxies. Delays prevented his starting this program before his retirement in 1942. When Shane became the director in 1945, no other Lick astronomer was interested in the program, and he decided to undertake it himself. He felt that the observatory, in accepting the Carnegie gift, had made a commitment to continue the project. The astrograph had been completed and erected under Wright's direction. Shane made the final optical adjustments of the astrograph, then started photographing the sky. Shane and his assistant Carl A. Wirtanen took a total of 1,246 acceptable plates between 1947 and 1954, covering about 70 percent of the sky on 17 × 17-inch photographic plates, each depicting a 6° × 6° area. In order to measure the stellar proper motions, a second set of photographs had to be taken a few decades later. In addition, in response to a request by Dutch astronomer P. J. van Rhijn, Shane and Wirtanen took photographs of 139 Kapteyn Selected Areas, from declination -15° to the North Pole, on 10 × 10-inch plates.

Instead of sitting and waiting until the second-epoch observations could be started, Shane decided to carry out the enormous task of counting all the galaxies recorded on the plates. He had two reasons for beginning this program. First, previous knowledge on the distribution of galaxies was based on counts by Edwin Hubble and others in small, discrete areas of the sky. They gave only a general idea of the distribution without any possibility of detecting fine structure within it. Thus there was an important research problem waiting to be carried out. Second, the long-term program, involving much routine counting, could be planned so as not to interfere with his administrative duties as director. He could do part of it himself.

Prior to the counting, Wirtanen had to inspect each plate to judge its acceptability. In this process he discovered a num ber of new comets. Then he and Shane counted the galaxies nearly in step with the taking of the photographs. Quite early in the program Shane noticed pronounced clustering in the distribution of galaxies as had been reported earlier by Harlow Shapley. Shane invited Berkeley statisticians Jerzy Neyman and Elizabeth L. Scott to make a statistical investigation of this phenomenon. They suggested extending the proper-motion program southward for statistical purposes, and Shane and Wirtanen photographed an additional 144 fields. Neyman and Scott's analysis, jointly with Shane, showed that not only clusters of galaxies, but also aggregates of clusters exist in the universe. The aggregates were called clouds by Shane, but are presently known as superclusters. With Gerald E. Kron, he carried out photoelectric studies of galaxies. They confirmed Walter Baade's result that the previous photographic photometry by Hubble, based on standards in Selected Areas, was in error by almost one magnitude. Shane and Kron derived new data for the galactic extinction and from their measurements drew refined boundaries of the zone of avoidance of galaxies.

Shane and Wirtanen published counts of the numbers of detected galaxies in each square degree of the sky covered by their photographs. They had done the actual counting in 10' squares; the total number of one-and-a-half million such squares shows the immensity of work involved and the impracticality of publishing the counts in detail. Later, however, the complete and detailed numbers were transferred to magnetic tapes by P. J. E. Peebles at Princeton. Peebles recognized that the counts were a gold mine for cosmological studies of structure in the universe, being the only existing statistically uniform, comprehensive set of data covering a large fraction of the celestial sphere. The main result to emerge from Peeble's theoretical analysis was that the galaxy clustering shows no characteristic length scales. The covariance function is a power-law out to very large distances. This suggests that the clustering grew out of a scale-force distribution of small density irregularities produced in the "Big Bang." Peebles derived many interesting new results on the distribution of galaxies from these detailed counts. Thus Shane and Wirtanen's publications inspired other researchers to analyze and discuss their data.

After the whole set of 1,246 photographs had been taken with the 20-inch Carnegie astrograph, Shane decided to photograph the sky again, with a smaller-aperture, wider-field telescope that would not reach objects as faint as those recorded during the proper motion program. Counts of galaxies on these plates would give information on the distribution of galaxies at a brighter magnitude limit. He borrowed a Ross five-inch lens from Mount Wilson Observatory and took all the photographs, but then decided to forego the counting. This set of photographs, however, known as the Lick Sky Atlas, turned out to be quite useful to astronomers as a reference atlas. Many copies have been distributed in the United States and abroad. An extension of this atlas to the Southern Hemisphere was carried out at Mount John Observatory of the University of Canterbury, New Zealand.

ADMINISTRATION

Shane's important contributions to science were by no means limited to his personal research. At Berkeley, Shane lunched regularly at the Faculty Club, the center of the professors' informal activities in the years between the wars. He was personable, intelligent, hard working, and absolutely trustworthy. He became acquainted with faculty members from all over the campus, and many of his friends later became department chairmen, directors, and deans. One friend, Commander Chester W. Nimitz, organized the first Naval Reserve Officers Training Corps unit in the country at

Berkeley in 1926, which he headed for three years before being reassigned to sea duty. Years later, as the victor of the Pacific Sea War, he became Fleet Admiral Nimitz. He was appointed a University of California Regent in 1948 and chairman of the Lick Observatory Committee in 1951.

Shane's friends quickly became aware of his interest in university affairs, particularly those concerned with academic excellence. In consequence he was appointed to the Committee on Schools, which visited California high schools and evaluated them as sources of students for the University of California. Later he served on the Budget Committee, whose decisions are crucial in faculty promotions, first as a member and later as chairman, and then on the Committee on Courses. He was elected vice-chairman of the Academic Senate and presided whenever the ex-officio chairman, University president Robert G. Sproul, was absent. Sproul and Shane cooperated closely until 1958 when they both retired.

In 1942, Ernest O. Lawrence, recognizing Shane's talent in administration, asked him to take over some of the responsibilities of the wartime work going on in his Radiation Laboratory. Later, at the personal request of General Leslie R. Groves, Shane went to Los Alamos as assistant director for scientific personnel under J. Robert Oppenheimer. Shane's calm manner, impeccable conservative credentials, and wide acquaintance among scientists were important qualifications for both these posts. When he witnessed the first test of the atomic bomb, at the Trinity site near Alamogordo on July 16, 1945, he knew the war would soon be over.

When Wright had retired as director of Lick Observatory in 1942, President Sproul had asked Shane to assume the post. He had declined the offer because of his wartime duties, recommending that Joseph H. Moore, already sixty-four years old, be appointed for the duration of the war. After Hiroshima, Sproul renewed the offer and Shane accepted.

He took up the post late in 1945. One of the first things Shane did as director was to begin holding staff meetings to discuss and seek advice on the future of the Observatory, as well as on current problems. This was a major departure from the previous rather autocratic regimes. Shane's leadership was particularly prominent in the design and construction of the 120-inch telescope, then the second largest in the world. By the time of his retirement from the directorship in 1958, it was nearly ready for regular operation.

From the days of W. W. Campbell, every Lick director had recognized the need for a new large reflecting telescope to put the Observatory back at the frontier of observational research. Campbell, Robert G. Aitken, Wright, and Moore had each in his turn tried to obtain the necessary funds. Shane, during his years in Berkeley, had probably discussed the idea with Sproul. In the early days of World War II, the president included the telescope project in the University of California's huge, ten-year building program planned to begin after the war.

Sproul wanted Shane to take charge of the advance planning for the telescope. The Los Alamos administrator managed to do so by correspondence and in one quick trip to California in March 1945. He headed a committee whose members he himself had recommended to the president. They included Joseph H. Moore; Nicholas U. Mayall, then a young Lick staff member on leave for wartime technical work in Pasadena; Walter S. Adams, director of Mount Wilson Observatory; and Ira S. Bowen of the California Institute of Technology. Shane's basic strategy was to use as much as possible of the Pasadena expertise and experience gained on the 200-inch project and to preserve the California money for building the telescope. John A. Anderson, who had supervised the Palomar telescope project, also met with the committee, and Walter Baade provided copious advice. Mayall and Gerald E. Kron, another Lick staff member on leave for war work in Southern California, pressed intensively for as large a telescope as the available money would buy. Shane supported them and the decision was quickly reached to go for a 120-inch reflector.

As soon as the two atomic bombs had been dropped and it became clear that Japan would surrender, Shane resigned his Los Alamos post and hurried back to California. From then on much of his time, even before he formally took over the Lick directorship on December 1, 1945, was concerned with making the telescope a reality.

He immediately became involved in defending the telescope budget item before the Legislature, which had first deleted it then, after some politicking between the senators and the governor, restored it and passed the bill. Next Shane had to hire engineers, familiarize them with astronomical requirements, and supervise their work. Prior to the construction of the telescope, he directed the building of its dome, including the optical shop and testing facilities. He had to go back to President Sproul several times for additional funds when costs outran the early plans. Shane hoped to have the telescope operational before his retirement from the directorship but encountered delays. His successor, Albert E. Whitford, headed the telescope's completion.

Since galaxies constituted one of the important research topics at Mount Wilson and Palomar Observatories, Shane was instrumental in arranging regular informal meetings between their astronomers working in this field and those at Lick. The meetings were held for a number of years, alternately at Mount Hamilton and in Pasadena. In these discussions, Hubble encouraged Shane to undertake the counting of galaxies. In 1948 Shane recommended Hubble very strongly for a University of California honorary degree, writing that "no living astronomer has done so much as he to enlarge and clarify our views of the universe as a whole." The following year the Lick director escorted Hubble to the Berkeley graduation ceremony where the University conferred an honorary doctorate of laws on the great observational cosmologist.

Shortly before his retirement from the Lick directorship, Shane was appointed to the Board of Directors of the Association of Universities for Research in Astronomy (AURA). He served as chairman of its Scientific Committee until 1959, when he became president. He was thus among AURA's leaders during its early years, including the founding of Kitt Peak National Observatory with headquarters in Tucson, Arizona, and the inception of Cerro Tololo Inter-American Observatory in Chile. He was a close friend of Robert R. McMath, the first president and later chairman of the board of AURA. Shane traveled to Chile several times as an advisor in the selection of the site for the planned observatory.

Shane strongly recommended Nicholas U. Mayall for appointment as the second director of Kitt Peak National Observatory, to succeed Aden B. Meinel. Mayall left Lick to accept the position in 1960. In his first years at Kitt Peak, he depended heavily on Shane for advice and counsel. They had frequent telephone discussions, and after Shane left the AURA board in 1962 they corresponded regularly on a personal basis until his death.

Shane was also particularly interested in helping to develop astronomy in New Zealand. While still director, he invited Ivan Thomsen from the Carter Observatory in Wellington to Lick to familiarize himself with research at a major astronomical institution. In subsequent correspondence and personal meetings, especially with Frank M. Bateson, Shane urged a site survey in New Zealand for a possible new observatory. The survey was carried out and ultimately an observatory was established on Mount John, in a cooperative ar rangement between the University of Canterbury and the University of Pennsylvania.

ECHELLE SPECTROGRAPH

It is not generally known that Shane first suggested the idea of the astronomical echelle spectrograph, essentially in its present-day form. He did this in 1946, when he and other Lick astronomers were planning the 120-inch reflector. Shane wanted to equip the telescope with a high-dispersion instrument for stellar spectroscopy but hoped to avoid building a coudé focus like that used for this type of work at Mount Wilson and planned for Palomar. Instead he wished to design a high-dispersion spectrograph to be used at the Cassegrain focus, behind the primary mirror. Such an arrangement would save starlight and money and avoid several complications in the design of the telescope. Shane realized that a medium-dispersion spectrograph, the type traditionally placed at the Cassegrain focus, could not simply be scaled up to give the high-dispersion that a coudé spectrograph could provide.

From his experience in solar line-profile work and laboratory spectroscopy, Shane was aware of the "echellettes" that had been developed by Robert W. Wood at Johns Hopkins University. They were essentially coarse reflection gratings, ruled with a blaze that concentrated their light into high spectral orders, giving high angular dispersion. Laboratory spectroscopists used them, as Shane knew, to get very high dispersion and thus resolve the fine structure of individual spectral lines.

He realized that, combined with only a moderate focallength camera, such an echellette could provide the high dispersion needed by astronomers in a relatively small instrument, which could be mounted at the Cassegrain focus. However, the difficulty was that an echellette, since it worked in a high spectral order, necessarily produced not a single long spectrum, but rather one composed of many overlapping orders. This was no problem in the laboratory, where a single emission line could be studied with very little danger that another line from a different order would accidentally coincide with it. It would be fatal for stars with continuous spectra.

Shane's solution was to cross the echellette with a small prism, which would provide just the right amount of deviation perpendicular to the main dispersion to separate the different orders. Thus several thousand Angstrom units of spectrum could be mapped out in many orders onto a single rectangular photographic plate. In this way the best field of the optics would be effectively utilized, and a large spectral range could be photographed in a single exposure with minimum light loss. Previous laboratory spectroscopists had occasionally used cross-dispersion to get rid of unwanted orders but no one had ever mapped out the spectrum in a two-dimensional format like this.

Shane wrote Wood in April of 1946 outlining these ideas and providing a specific numerical example of the design. He asked for the laboratory spectroscopist's comments and inquired whether he could provide a suitable echellette. Shane followed up his letter with a visit to Wood's laboratory in Baltimore in May. That summer Wood set up a trial version of the system in the barn of his vacation retreat on Long Island and tested it visually with sunlight. The whole solar spectrum from the violet to the red was mapped out between the twelfth and seventeenth orders and despite "a rather poor echellette," wrote Wood, "[i]t looks like an awfully good idea to me." He later recorded the solar spectrum photographically with this system.

He presented a paper on this "new method of employing echellettes" at the meeting of the Optical Society of America in New York that fall. In both his oral presentation and his later written version of the paper Wood credited Shane with the original idea.[1] Spectroscopist George R. Harrison, who was presiding at the session at which Wood presented this paper and who, according to the latter, "said that he considered this the greatest advance in spectroscopy since the invention by Rowland of the concave grating!", took up the idea and pushed it further. Harrison, at his Massachusetts Institute of Technology spectroscopy laboratory, was developing very similar "echelles," and he discussed in detail the design considerations for using them most effectively to obtain a large spectral range at high dispersion. In his published papers he also generously credited Shane with the original suggestion.[2] Among other items, Harrison stated that a prism (which Shane had originally suggested) is more effective as the cross-dispersing element than a grating (which Wood had used).

The novelty of Shane's idea illustrates his wide range of knowledge and quick mind. In 1946 it was ahead of its time, however, for neither echellettes nor echelles could be obtained that were large enough and suitably blazed. Shane was not able to build a Cassegrain echelle spectrograph for the 120-inch reflector. Instead, a very good coudé spectrograph was constructed, under the supervision of George H. Herbig, to provide high dispersion. More recently, however, echelle spectrographs have been put into use on many astronomical

[1] R. W. Wood, "Concave Replica Gratings, and a New Method of Employing Echellettes," *Journal of the Optical Society of America*, 36(1946):715; "The Use of Echellette Gratings in High Orders," *Journal of the Optical Society of America*, 37 (1947): 733-37.

[2] G. R. Harrison, *Physical Review*, "The Production of Diffraction Gratings. II. The Design of Echelle Gratings and Spectrographs," 39(1949):522-28; G. R. Harrison, J. E. Archer and J. Camus, "A Fixed-focus Broad-range Echelle Spectrograph of High Speed and Resolving Power," *Journal of the Optical Society of America*, 42(1952): 706-12.

telescopes, including the Shane 120-inch, usually for moderate dispersion rather than for high.

OTHER ASPECTS

During Shane's many years on the Berkeley faculty, he spent more time on teaching than on research or administration. He taught considerably more than would normally have been expected of him, and he considered it the most important and rewarding part of his work. He was a good teacher, and as the University of California was one of the leading centers of graduate work in astronomy in the world, in his astrophysics classes he taught many students who later became outstanding researchers. Among them were, as undergraduates, Olin C. Wilson and Lawrence H. Aller, and as graduate students, Louis Berman, Fred L. Whipple, Nicholas U. Mayall, Daniel M. Popper, Horace W. Babcock, and Gerald E. Kron. Shane was also pleased to have attracted many of the best physics students—some of whom later became quite famous—to his astrophysics course. One, who remained his lifelong friend, was Edward U. Condon.

Shane had many interests outside astronomy and science. He was a longtime member of the Chit-Chat Club in San Francisco, a group of men interested in the arts, science, and current affairs. He was deeply interested in all things Icelandic, especially Icelandic literature and more particularly the sagas. Shane made two long visits to Iceland in 1967 and 1968, traveling around much of the island. He had several discussions of ancient Icelandic history with Kristian Elojarn, the director of the National Museum in Reykjavik in 1967, who had become president of the country by the following year.

Shane was an avid reader. He had a deep interest in biographies of world leaders and in both world history and the history of California—especially of the Auburn, San Fran cisco, Mount Hamilton, and Santa Cruz regions where he had lived. He was a raconteur of the first order, with an apt story for every occasion.

FAMILY LIFE

Donald and Mary Shane were an exceptionally close and cooperative married couple, and Mary had an important role in Donald's personal and professional life. As Mary Lea Heger she graduated from the University of California in 1919, and she received her Ph.D. degree in astronomy in 1924. In her thesis work at Lick Observatory she detected the presence of sodium atoms in interstellar space, a major discovery. She did not pursue an astronomical career, however, being fully occupied first with raising two small children, then later as the director's wife, with the duties of being the hostess at Lick Observatory. On remote Mount Hamilton there were many important scientific visitors from the United States and abroad. Throughout her experiences with them she retained her strong interest in astronomy and a particular attachment to Lick Observatory.

When Donald Shane was chairman of the Local Organizing Committee for the General Assembly of the International Astronomical Union, held at Berkeley in 1961, Mary carried a heavy load. She planned, organized the office work, and made arrangements for entertaining more than seven hundred participating astronomers—a total of about a thousand guests including spouses. An official record of thanks to Donald and Mary Shane can be found in the *Transactions of the International Astronomical Union*, which quotes Dr. Alena G. Massevitch, speaking for the visitors from abroad: "No words of mine can convey adequate thanks to them for their arduous efforts over many months; the success of these efforts is clear from the perfection of the organization, and our appreciation is unlimited."

Mary Shane also demonstrated her organizational talent and devotion in establishing the Lick Observatory Archives, renamed the Mary Lea Shane Archives in 1982. She conceived the idea of converting the old Lick Observatory files, dating from 1876, into an organized source of historical information. She began the project on Mount Hamilton. It reached its full fruition when the Lick headquarters were moved to the new Santa Cruz campus of the University of California in 1966. Mary Shane persuaded Chancellor Dean E. McHenry and University Librarian Donald T. Clark to provide space for the Lick Archives in the University Library. Under her leadership and with her active participation, a group of dedicated volunteers identified, classified, and catalogued thousands of letters, clippings, and photographs. Letters from almost every notable American astronomer since Simon Newcomb, as well as from many European scientists, can be found in the Shane Archives.

RETIREMENT YEARS

After retirement Donald and Mary Shane lived at their home in the redwoods at Scotts Valley, near Santa Cruz. Their American and foreign friends, mostly astronomers and their families, frequently visited them. The Shanes had a swimming pool and a separate guest house for their visitors. In the years 1962 through 1965, the University of California, Santa Cruz, campus physical plan was being formulated, and Chancellor McHenry frequently sought Shane's advice. As an emeritus faculty member, Shane served on the Campus Planning Committee for two of those early years. He was a regular participant in informal meetings of the Santa Cruz faculty emeriti group. Its members enjoyed listening to Shane's reminiscences, drawn from his exceptional memory and flavored with his characteristic wit and humor. He recollected many events and noted personalities from his seven decades of association with the University of California.

Leukemia finally slowed him down, and he died at the age of eighty-seven on March 19, 1983. His wife Mary died of a heart attack on July 13, 1983, her eighty-sixth birthday. They are survived by their sons Charles Nelson Shane, presently associate dean at the Fletcher School of Law and Diplomacy of Tufts University, Massachusetts, and William Whitney Shane, a professor and radio astronomer at the University of Nijmegen in the Netherlands, as well as by six grandchildren and three great-grandchildren.

Honors were bestowed upon Donald Shane for his many achievements. He was elected to the American Philosophical Society in 1955 and to the National Academy of Sciences in 1961. He was awarded an honorary LL.D. degree by the University of California in 1965, and the 120-inch telescope that he initiated was named after him in 1978. Shane was an Associate of the Royal Astronomical Society and of the Royal Astronomical Society of New Zealand. The minor planet 1961 TE, discovered at Goethe Link Observatory, Indiana University, was named (1994) Shane in his honor in 1981.

WE ARE GRATEFUL to archivists at the Niels Bohr Library of the American Institute of Physics and at the Mary Lea Shane Archives of Lick Observatory for making available their rich stores of information for this biography. Transcripts of several interviews Donald Shane gave to historians were especially useful, as were his own handwritten autobiographical notes, composed in the last years of his life. His published scientific papers and our personal recollections provided supplementary sources.

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William Christopher Stadie

June 15, 1886-September 12, 1959

By Isaac Starr

Few investigators have been so consistently productive as William Stadie. His life work can be most easily presented by dividing it into three parts. In the first, his attention was focused on the cyanosis so conspicuous in patients with influenza; he was the father of oxygen therapy. In the second—responding to the needs of World War II—he was chiefly concerned with oxygen toxicity. In the third, Stadie made major contributions to our knowledge of the abnormalities of carbohydrate metabolism and diabetes.

For many years, Bill Stadie and I had adjacent laboratories on the eighth floor of the Maloney Building of the University Hospital and we usually lunched together. He was one of my oldest medical friends.

Bill had an unusually difficult time completing his medical education. Believed to have pulmonary tuberculosis as an adolescent, he was taken out of school and sent to work on a farm for a year. When this episode was evaluated later by experts in the diagnosis of tuberculosis, using both his old and more recent chest X-rays, all agreed that Stadie had never, in all probability, had TB at all. But the episode cost him a year of his working life. In addition, he had to earn money by teaching school for several years before he was able to finish college at New York University, from which he took his degree in 1907.

Stadie liked to boast, with a twinkle in his eye, that he had put himself through medical school at the College of Physicians and Surgeons (which granted him the M.D. degree in 1916) by writing a textbook of pathology. If listeners expressed suprise at so major an accomplishment by so young a man, they soon learned that Bill had helped finance his education while a medical school undergraduate by typing the manuscript of McCallum's well-known pathology text.

After a stint in the Army Medical Corps during World War I, Stadie's successful internship at the Presbyterian Hospital won him a research job at the Hospital of the Rockefeller Institute, where a group was being organized to study the newer treatments of syphillis. But before this study could get off the ground, the great influenza epidemic paralyzed the country.

In many influenza cases, cyanosis of bronchial pneumonia was a conspicuous symptom. After learning the new techniques of blood-gas analysis from Van Slyke (who had just originated them), he worked to perfect techniques of arterial puncture—experimenting first with animals, then on himself and other volunteers, and finally on his patients—proving to the satisfaction of everyone that arterial puncture, long thought by clinicians to be a dangerous procedure, was harmless in skilled hands. Many give Stadie the credit for the first arterial puncture on a patient, but I often heard him deny, with characteristic modesty, that he had been first, insisting rather that Hurter, a German researcher, had preceded him.

Having introduced the arterial puncture in clinical medicine, Stadie was able to make pioneering studies of lung function in his patients by comparing the oxygen content of the air inhaled with that of arterial blood. This technique allowed him to demonstrate that the cyanosis was due to arterial anoxemia of a dangerous severity. Studies on the effectiveness of various methods of treating cyanosis followed, and Stadie soon found that anoxemia could be overcome by breathing air enriched with oxygen. He then supervised the construction of a small, gas-tight room in the Rockefeller Hospital with controls for oxygen, carbon dioxide, moisture, and air temperature that permitted bed patients to breathe the desired concentrations over long periods without the discomfort of masks and nose-pieces. The principles of Stadie's chamber formed the basis for the oxygen chambers and tents that have since become routine hospital equipment.

After four productive years with the Rockefeller Hospital, Bill Stadie moved to Yale, where Francis Blake was putting new life into the Department of Medicine. He served on Yale's medical faculty from 1921 to 1924, then came to the University of Pennsylvania. He was appointed John Herr Musser Professor of Research Medicine in 1941. In 1944 he served with the Office of Scientific Research and Development of the United States Public Health Service. Though he had retired from teaching in 1956, Stadie continued as the Musser Professor Emeritus and was actively engaged in research at the time of his death, at the age of seventy-three, in 1959.

After his groundbreaking discoveries in oxygen therapy and his introduction of the arterial puncture into clinical medicine, Stadie moved on to investigate oxygen toxicity—a concern of the military during World War II. He extended his researches to the combination of oxygen and carbon monoxide with hemoglobin and assisted in clarifying the roles of the carbamino compounds and of carbonic anhydrase in accelerating the shifts of carbon dioxide to and from the blood. Stadie contributed refinements of methods for blood-gas analyses, determinations of hemoglobin, methomoglobin, fixed-base cations in blood, and an electron-tube potentiometer for blood pH measurements.

During his researches he discovered a discrepancy in the data then available on the supposedly well-understood pro cess of oxygen and CO_2 exchange in blood. According to his findings, much more CO_2 emerged from the blood during its passage through the lungs than the views of physical chemistry of blood then current could account for. To interpret this unexpected finding, new techniques were needed: those of enzyme chemistry to measure enzyme activity and those of radioactivity to locate the enzymes in tissues and identify the sources of their metabolic byproducts. Stadie not only mastered these new techniques, he added considerably to our knowledge of abnormalities in carbohydrate metabolism—work for which he was particularly suited by his unusual facility with mathematics.

He was the first to label insulin with radioactive tracers and to demonstrate that a high-affinity binding of the hormone to its target tissue was required for its biological effects. More than two decades later, quantitative studies of insulin-binding have fully confirmed Stadie's observation.

He further demonstrated that the hyperketonemia of animals with acute experimental diabetes results primarily from hepatic overproduction of ketone bodies rather than from a defect in their utilization. Stadie adduced an important part of the evidence on which presently accepted views regarding diabetes are based: that the liver splits fats almost quantitatively into acetoacetic and hydroxybutyric acid, which are circulated to the other tissues for combustion; that the muscles of a diabetic can burn acetoacetic acid at a normal rate; and that excretion of acetoacetic and hydroxybutyric acids occurs in diabetes—when carbohydrate is not available for combustion—because these acids are formed faster than the tissues can burn them.

Any tribute to Bill Stadie as a scientist would be incomplete without a tribute to him as a man. His talents were not limited to research. He ran a happy and successful laboratory—as his many associates, graduate students, and techni cians are glad to attest. Those of us made welcome in his home often paused to admire the beautiful mahogany furniture and were surprised to learn that he had made the pieces himself. He played both the cello and the clarinet—if not well, well enough to enjoy it—and great music always delighted him. Outside his house was his carefully tended garden, bordered by a row of beehives.

The quality of the man and his work have been recognized everywhere. He was an editor of the *Journal of Biological Chemistry* for many years and was editor-in-chief of the American Diabetes Association journal, *Diabetes*, for the last three years of his life.

Elected to the National Academy of Sciences in 1945, Stadie received the Alverenga Award of the Philadelphia College of Physicians in 1957, the Phillips Medal of the American College of Physicians in 1941, the Kober Medal of the Association of American Physicians in 1955, and the Banting Medal of the American Diabetes Association in 1956. He acted as a consultant to the National Institutes of Health's Division of Metabolic Diseases. He was a member of the American Philosophical Society, the American Society for Clinical Investigation, the American Society of Biological Chemists, and the Association of American Physicians and received the honorary degree of doctor of science from the University of Pennsylvania in 1959.

He married Amanda Brugger, who was working in the library at Yale while he was on the faculty there. Their daughter was a constant source of delight to them both. The death of his first wife from a brain tumor was so devastating to him that his friends feared he might not recover, but he eventually did, and his second marriage to Catherine Tyler was also a happy one.

Throughout his active years and even after his retirement he never showed signs of the mental rigidity that so often comes with age. During his later years—despite considerable ill health—his mind remained as fertile for new ideas as in his younger days. He also took an interest in his fellow man and—poor himself in his youth—was greatly concerned with social problems of the poor.

Suffering from mild angina pectoris occasionally for several years, he died of a heart attack. His refined experiments, which so much advanced his fields of interest, will live long after him.

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