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ERIC GLENDINNING BALL

1904—1979

A Biographical Memoir by

JOHN M. BUCHANAN AND A. BAIRD HASTINGS

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Biographical Memoir

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Eric S 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 ^{14}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 first-hand 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 Willstätter, 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 mater, 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 do Cruzeiro 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 byproduct 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 Ozone, 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, Harvard Medical School
1958–1959
1944–1946 Secretary, Biochemical Panel, Board for Coordination of Malarial Studies, Washington
1945 Visiting Professor, University of Brazil Medical School
1945 Ordem du Cruzeiro 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 Vis-
iting Investigator, Scripps Clinic and Research
Foundation, La Jolla California
- 1964 Commonwealth Fund Fellow, Brazil. Visiting Profes-
sor, 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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