Hermann J. Muller

Genes, Radiation and Society. The Life and Work of H. J. Muller. ELOF AXEL CARLSON. Cornell University Press, Ithaca, N.Y., 1981. xiv, 458 pp., illus. $29.95.

In 1926, while at the University of Texas, Hermann J. Muller began a series of experiments irradiating fruit flies with x-rays. In short order he found a total of 100 lethal and visible mutations, twice the number that had been detected by all *Drosophila* workers since Thomas Hunt Morgan had happened on his white-eyed mutant 16 years earlier. At a conference in Berlin in 1927, Muller reported fully on his results and created a sensation. In Curt Stern's recollection, the audience recognized that they had been "privileged to be present at the moment of a decisive advance in man's probing of nature, the first time that he had willfully changed the hereditary material" (p. 150, note 32). Not only the possibility of such change but the fly stocks and techniques that Muller had developed to bring it about opened a new branch of genetics, fundamentally important in its own right and for its bearing on the social issues raised by radiation. In 1946 Muller was awarded the Nobel prize. Now Elof A. Carlson has given us this first biography of Muller, an important book as well as an absorbing narration of the life of the father of radiation genetics.

And quite a life it was. Muller's family had come to the United States after the German revolution of 1848. His father, the coproprietor of an art metal firm in New York City, was a socialist more interested in intellectual matters than in business, an apostate Catholic, liberal in religion, and above all, a Darwinian. The familial predisposition was fortified during Muller's undergraduate days at Columbia University, where, as Edgar A. Altenburg, a lifelong friend and fellow scientist, recalled, Muller "traded in the three R's for the three S's—science, sex, and socialism" (p. 33).

The science first centered on the work of the physiologist Jacques Loeb, whose writings Muller read independently, and the cytologist Edmund B. Wilson, under whom he studied. Loeb's books convinced Muller of the physicochemical basis of biological processes, and Wilson inspired in him a vigorous commitment to the chromosomal basis of heredity. He brought both beliefs to Thomas Hunt Morgan's fly room, where he started to work while still an undergraduate and where he took his Ph.D. In 1915 he was one of the four coauthors, at age 25, of Morgan's celebrated classic, *The Mechanism of Mendelian Heredity*. By the time Muller joined the Texas faculty in 1920, his attention had already shifted from the chromosome to the gene. Thinking that the nature of the gene might be gotten at through mutations, he took up the program of mutation research that led to the triumph of 1926–27 and ultimately to the Nobel prize.

In 1932 Muller left Texas—never to return, as it worked out—on a Guggenheim fellowship for Berlin. Revolted by the virulent anti-Semitism—Muller considered himself part Jewish by virtue of his mother's remote Sephardic ancestry—he moved in September 1933 to the directorship of the genetics laboratory in the institute of N. I. Vavilov in Moscow. During his three years in the Soviet Union, he was drawn into the increasingly vitriolic, ultimately deadly dispute that pitted Lysenkoism against so-called Mendelism-Morganism. The more Muller witnessed the arrests, disappearances, and false confessions of his scientific friends and colleagues in Stalin's Russia, the more disillusioned he grew with the U.S.S.R. He left in 1936, after service in a Loyalist blood unit in the Spanish Civil War, moving to the University of Edinburgh, then in 1940 to the United States, and in 1945 to Indiana University as professor of biology. The professorship, together with the Nobel prize money in 1946, brought him the first financial security of his mature life, yet Muller, his passionate social concern undiminished, hardly sat back to rest on his laurels. From the immediate postwar period to his death in 1967, he was actively involved in the issues of nuclear fallout, nuclear war, the social responsibility of science, and the special brand of positive eugenics that he dubbed "germinal choice."

Carlson provides an intimate portrait of Muller's life and work. He has drawn fully on the published writings, a few key interviews, and, most important, the extensive Muller archive of correspondence and manuscripts at Indiana University. A biologist and an accomplished historian of genetics, Carlson here treats with admirable illumination and accessibility the lifetime development of Muller's scientific work. He identifies Muller's contributions to classical and human genetics, particularly the concept of genetic load. He convincingly stresses Muller's early advocacy of the physicochemical study of the gene as the key to heredity. A former student of Muller's, Carlson admires his subject, especially the rationalism and commitment to the social responsibility of science. With justification he gives a good deal of attention to the political concerns which, throughout his life, were as important to Muller as his science.

Muller never made a secret of his left-wing sympathies. In 1932, in a widely reported speech, he denounced the crude, racist, American program of negative eugenics, declaiming that economic interests dominated eugenic concerns. The Texas administration called him to account for having sponsored a pro-Communist student journal before he left for Berlin; in 1936 he resigned from the university rather than submit to an inquiry on the matter. In the Soviet Union that year, at a meeting of the Lenin All-Union Academy of Agricultural Sciences, he boldly declared that to opt for either so-called Morganism-Mendelism or the doctrines of Lysenko was to be "confronted with a choice quite analogous to that between medicine and shamanism, between astronomy and astrology, between chemistry and alchemy" (pp. 231–232).

From 1936 onward, Muller regarded the Soviet Union as a brutal, intolerant dictatorship. In the early postwar years, he defended the ongoing development of the American nuclear arsenal, supported the California Loyalty Oath, and argued that avowed Communists ought not to enjoy the protections of academic freedom. While Muller had long warned against the genetic hazards of low-level radiation, he declined for many years to endorse an end to nuclear testing. To him the issue was nuclear war, a prospect of far greater peril than the comparatively few deaths and diseases statistically certain to arise from atmospheric testing. Yet in 1956 he changed his mind. Muller called for an end to testing on grounds that it was escalating the arms race. He participated in the first Pugwash meeting. And even though he continued to doubt the threat of radiation from testing, he even signed a petition circulated by Linus Pauling that called for an end to weapons tests because of

the hazards of fallout. He did so, Carlson informs us, because he feared that if he did not sign he would by implication be identified on the nuclear weapons issue with the camp of Edward Teller.

Carlson supplies the reasons, as Muller offered them, for the shifts and turns in his political thinking. But one wishes that he had stepped further back and attempted to locate his mentor in political time and space, to compare his views on the nuclear arms race with those of other scientists, and, more important, to assess his political odyssey from the 1930's against that of others on the old pro-Soviet left. Muller's socialism seems to have taken more of a vaguely utopian than a concrete programmatic form. He read little in socialist theory. His only full work on social issues was his 1935 book *Out of the Night*, in which he advocated equal rights for women, birth control, abortion, miscegenation, and a positive eugenics—the germ of germinal choice—that hinged on artificial insemination with the germ plasm of men of high intelligence, cooperative attitudes, and longevity in good health. That the "so-called eugenics of the past was so mistaken . . . ," Muller once said, "is no more argument against eugenics as a general proposition than, say, the failure of democracy in ancient Greece is a valid argument against democracy in general" (p. 397).

Carlson portrays Muller the political idealist as responding rationally, if at times wrongly, to events. Yet people rarely come to political judgments through isolated cerebral analysis. One would like to know more about Muller's associations, friendships, involvements; about who, in addition to what, influenced him from the mid-1930s on. There are numerous subtle issues raised by Muller's political life that go far beyond his having "erred," as Carlson puts it, in taking the Soviet experiment under Stalin as the hope of the future. Though he left Russia in 1936, Muller did not publicly condemn Lysenkoism or the persecution of Soviet geneticists until 1948. Carlson reports that Muller refrained from speaking out all that while for fear of jeopardizing his remaining Soviet colleagues and of inviting charges from the left of being pro-Facist or anti-Soviet. The two reasons were far from equivalent. Carlson does not come to grips with the merits of Muller's silence, with the quality—as distinct from the rightness or wrongness—of his political judgment, or with the wisdom of his overall performance as a socially committed scientist.

As for his professional perceptions, Carlson tends to take Muller's point of view that he was often mistreated by colleagues, particularly by the Morgan group. Without doubt by the 1930's Muller had come to believe that Morgan, A. H. Sturtevant, and at times even C. B. Bridges had stolen his ideas, failed to give him proper credit for his contributions to the early *Drosophila* work, and blocked his professional advancement. The belief was surely intense. In 1932, feeling isolated at Texas, recently passed over for election to the National Academy of Sciences (Sturtevant had been elected), his first marriage on the rocks, Muller walked into the woods and swallowed a roll of sleeping pills. Searchers found him sitting dazed in the hills the next day, with a suicide note that included a bitter attack on the "predatory operations of T. H. Morgan" (p. 174).

The question is whether Muller's later belief conformed with the earlier reality. Carlson's handling of the matter leaves one troubled. The documentary support for his argument dates from the 1930's and, especially, from after World War II. So does the oral evidence, including Muller's mid-1950's lectures and interviews decades after the events with Edgar Altenburg, who also felt aggrieved by Morgan's treatment. Carlson asserts that Muller could remember incidents and events long after the fact with astonishing accuracy, yet he does not supply confirmation of the claim. There seems to exist virtually no evidence from the time that Muller felt exploited by the Morgan group. (To be sure, the Muller papers contain scant material for the period 1915 to 1932, but Carlson did manage to obtain letters written during those years to Altenburg and Julian Huxley.) More to the point, in a lecture in 1921 at Cold Spring Harbor, Muller praised Morgan beyond what might have been required for a dutiful and cautious junior geneticist, calling him an inspiring example of indefatigable activity, good humor, and courage. "His simplicity and dazzling liveliness of character, his flashing wit together with astuteness in detecting the most vital aspects of work (in the field of Mendelism and mutation) at a time when many other biologists were ending up in blind alleys—these are the qualities which attracted to Morgan and his work a group of young people interested in new problems" (p. 124).

Carlson is persuasive that Muller was a uniquely valuable if sometimes irritating member of Morgan's group, insisting upon chromosomal interpretations when others were skeptical, boldly framing a priori hypotheses in the face of Morgan's tenaciously inductive empiricism, and ingeniously designing fly stocks and experiments to test theoretical suggestions. Yet why Muller, a 5-foot-2-inch bantam, always feisty, a brilliantly capable scientist, should have come to feel victimized by Morgan—and others—remains murky. Carlson acknowledges that Muller suffered to a degree from a "priority complex," that he was "subject to an insecurity that welled up in a competitive, often polemically expressed and self-defeating desire to prove the priority of his ideas and experiments." Yet Carlson, who passes casually over the suicide attempt in a page or so, leaves the nature of that insecurity, of its deeper psychological roots and the way they shaped Muller's professional and political life, unexamined. His aim was more modest—not to write a critical evaluation of Muller's life but to provide "an accurate account of what he did, what he believed in, and what his values were."

Carlson has certainly accomplished that much, and more. If Muller's politics and scientific career raise so many questions, it is because Carlson has provided ample material to provoke them. Despite his clear sympathy for his subject, he has exploited the rich biographical sources with discipline and an unflinching willingness to reveal Muller's warts and errors. The result is a lucid, at times eloquent, rendering of Muller's remarkable life and of the scientific field he did so much to create.

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Genetics

Mammalian Genetics and Cancer. The Jackson Laboratory Fiftieth Anniversary Symposium. Bar Harbor, Me., July 1979. ELIZABETH S. RUSSELL, Ed. Liss, New York, 1981. xiv, 328 pp., illus. $42. Progress in Clinical and Biological Research, vol. 45.

At the symposium of which this book is the proceedings, the Jackson Laboratory, with much-deserved pride, celebrated its 50th anniversary and 50 years of progress in mammalian genetics for which it is largely responsible. The 18 papers by staff members and friends of the laboratory are of overall high quality. The focus is naturally on the house mouse, but there are some commensal diversions, depicting parallel development in human genetics. Eicher describes the history of the linkage map of the mouse as well as ingenious new cytogenetic techniques, such as duplication-deficiency mapping, which permits

localization of genes to G bands. In a summary of the molecular genetics of globin genes in the mouse, Leder *et al.* beautifully explain the methods of recombinant DNA technology and the impact of the split genes and intervening sequences in evolution. Green describes future work in which classical and molecular genetics will be brought to bear to decipher why genes are arranged the way they are on chromosomes. So, the 50th anniversary of the Jackson Laboratory presented 3 kilobase pairs of mouse sequence, leaving the remaining 2.299997×10^6 for the next 50 years.

In a section on differentiation and developmental genetics, Papaioannou's paper on chimeras and Illmensee's on manipulation of the mouse embryo describe mind-boggling experimental achievements and approaches for analyzing how genes control development. Stevens's continuing intriguing study of teratocarcinogenesis exemplifies his ingenuity in finding genes that determine the formation of teratocarcinomas. In 1967, he found that 1 percent of strain 129 males developed testicular teratocarcinomas. Only one teratoma was found in 11,000 F_1 hybrids of strain 129, although in several other strains the effects of multiple genes were indicated. Stevens began looking for these genes and in 1973 discovered the gene "*ter*," which increased the incidence of spontaneous teratomas to 30 percent.

A number of papers deal with medical genetics. McKusick outlines the staggering progress of the last 20 years in defining genetic defects in humans. Lux *et al.* describe the hemolytic anemias in mouse and human that result from abnormalities in spectrin. Scriver compares inborn errors of metabolism in the two species. Coleman details the fascinating experiments on the effects of genes that determine obesity and diabetes in the mouse.

Immunogenetics is covered in three papers. Bodmer discusses histocompatibility gene clusters from several species. In a paper on the future of immunogenetics Snell discusses the biological significance of MHC polymorphisms. Heston describes the development and utilization of inbred mice in cancer research.

The symposium concludes with two papers on retroviruses. Baltimore reviews the Abelson virus, a defective retrovirus that carries a host-gene element, which when transcribed in cells transforms them. Rowe *et al.* describe the finding of integrated retroviruses in the mouse genome. It is remarkable and curious that roughly 0.1 percent of the 2.3×10^6 kilobase pairs in the mouse are thought to be retroviral sequences. These genes are directly or indirectly responsible for the high incidence of mammary tumors and leukemias in some inbred strains of mice.

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Interferon Popularized

Interferons. A Primer. ROBERT M. FRIEDMAN. Academic Press, New York, 1981. xii, 152 pp., illus. $17.50.

Not so long ago interferon research was a highly specialized, somewhat esoteric branch of virology familiar to a small group of aficionados. Most physicians and biologists were likely to have encountered the term "interferon" somewhere in the professional literature but otherwise had little awareness of its significance. To the layperson the term was very likely meaningless. The fact that Friedman deemed it appropriate to write a primer about interferons (and even managed to find a reputable publisher ready to print it) indicates how profoundly the perception of this field has changed in the last couple of years.

Friedman set out to write a book "for the student, scientist, physician, or educated layperson who wishes to know something about interferons." The book is of a rare sort—not quite an authoritative monograph or scholarly review and not really a textbook. In a style reminiscent of articles published in *Scientific American* Friedman explains what interferons are and describes their varied biological functions, activities, and possible medical applications.

Friedman develops the subject in a systematic, logical sequence. He describes the discovery of interferons by Isaacs and Lindenmann some 25 years ago. For the reader with no previous exposure to experimental work with interferons, a short chapter describes assay methods most widely employed in laboratory research. Other chapters describe how interferons are produced and purified. More than half of the book is devoted to a thorough analysis of the various actions of interferons, an evaluation of the role of interferon as a factor in the natural defense against viruses, and a realistic assessment of the possible clinical uses of interferons in viral infections and cancer.

Despite its compactness, the book contains a fair amount of technical detail, much of it highlighted by useful illustrations and summarized in simple tables. The subtitle of the book may be somewhat misleading: this is not a primer suitable for the reader totally uninitiated in modern biology, biochemistry, and immunology. Written in a refreshingly clear style and with a useful glossary of technical terms appended, the book will be most appreciated by science-oriented college students and physicians wishing to learn about the many ramifications of interferon research in biology and medicine.

Those reaching for this small book will not be shortchanged. One of Friedman's accomplishments is that he avoids oversimplified generalizations and cheap promises of miraculous curative powers of interferons while conveying some of his own excitement with this field of research.

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Biological Gerontology

Aging. A Challenge to Science and Society. Vol. 1, Biology. Papers from a conference, Vichy, France. D. DANON, N. W. SHOCK, and M. MAROIS, Eds. Published on behalf of l'Institut de la Vie and the World Health Organization Regional Office for Europe by Oxford University Press, New York, 1981. xvi, 346 pp., illus. $59.50.

This is the first of three volumes on the scientific, medical, and social aspects of aging that l'Institut de la Vie and the World Health Organization plan to produce. The volume, which is based on the proceedings of a conference held in 1977, contains 30 papers on topics ranging from theoretical gerontology and cell biology to the physiological aspects of aging. Most papers are reviews based to a large extent on the authors' own work, and few, if any, contain data not available elsewhere. Despite the international intent and European location of the conference, 43 of the 53 listed contributors are from the United States. One wonders whether this reflects American dominance in biological gerontology or whether other factors are operating.

Several sections of the book are particularly worthwhile. A 60-page section on the central nervous system is excellent. It includes discussion of age-related differences in brain anatomy, blood flow, and neurotransmitter activity as well as