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# HERMANN JOSEPH MULLER
1890—1967

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*A Biographical Memoir by*
ELOF AXEL CARLSON

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H. J. Muller

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*December 20, 1890–April 7, 1967*

BY ELOF AXEL CARLSON

HERMANN JOSEPH MULLER is best known as the founder of the field of radiation genetics, for which he received the Nobel Prize in Physiology or Medicine in 1946. He was also a cofounder—with Thomas Hunt Morgan, Calvin Blackman Bridges, and Alfred Henry Sturtevant—of the American school of classical genetics, whose use of the fruit fly, *Drosophila melanogaster*, provided a remarkable series of discoveries leading to an American domination of the new field of genetics first named in 1906 by William Bateson.[1] Muller's career as a geneticist was productive and included 370 publications and participation in active laboratories in Texas (the Rice Institute and later the University of Texas at Austin), the Soviet Union (at their National Academy of Sciences in Moscow and Leningrad, Muller being a corresponding member), Edinburgh (the Institute for Animal Genetics at the University of Edinburgh), and Bloomington, Indiana (in the Zoology Department at Indiana University).[2]

Muller was a controversial critic of society who made an effort to decry abuses of genetics and who served on many national and international committees as an advocate for radiation safety. He was both a critic and advocate of eugenics, denouncing the American eugenics movement for its racism, spurious elitism, sexism, and mistaken assumptions

on both the transmission of behavioral traits and the belief that many social traits were primarily innate. He promoted an idealistic eugenics throughout his life, believing that those with beneficial genes should have opportunities to transmit them. His early enthusiasm for socialism and communism cost him dearly later in life, despite his role as the leading world critic of the Lamarckian movement initiated in the Soviet Union by Trofim D. Lysenko.

## FAMILY AND EDUCATION

Muller was born in New York City on December 20, 1890. His friends knew him as Herman (the last *n* being dropped) until the 1940s, when he shifted to Joe on the recommendation of his second wife, Dorothea (née Kantorowicz) Muller. Professionally, he used his initials and his articles appear as H. J. Muller. Muller was a third-generation American. His father's ancestors came to the United States from Coblenz (the Rhine Valley) in Germany after the unsuccessful revolution of 1848, which they supported. Three Muller brothers came to the United States that year. One died the following year when he tried to make his fortune in the California gold rush. The other two brothers established themselves in an art metal business in New York City on Canal Street, preparing bas reliefs, frames, and other objects for the middle class homes of that era.

The Mullers were originally Catholic, but on H. J. Muller's side they became Unitarians, the religion of upbringing of H. J. Muller. They were also sympathetic to the emerging labor and socialist movements, an influence that carried over to the young Muller. On his mother's side (the Lyons) the family was originally from England of mixed Jewish and Anglican background. This less-than-half "Jewishness" Muller used on occasion to offer his solidarity with Jewish colleagues who were victims of anti-Semitism in the United

States or Germany. Muller himself was an atheist and later in life chose the American Humanist Association as an outlet for his religious feelings, serving as president of that organization in 1957.

On his uncle's side Muller's penchant for academic life was shared by his first cousin Herbert J. Muller (English critic and author of *Uses of the Past*) and first cousin Alfred Kroeber (anthropologist known for his studies of American Indian cultures). Alfred Kroeber's daughter became the well-known science fiction writer, Ursula LeGuin. Muller had two children. With his first wife, Jessie (née Jacobs) Muller, he had a son, David Muller, who became a professor of mathematics. With his second wife (she called herself Thea) he had a daughter, Helen Muller, who became a professor of marketing and public health. David Muller has continued the academic tradition with a son, Kenneth Muller, a professor of neurobiology. Helen has also continued the tradition with a daughter, Mala Htun, who is a professor of anthropology.[3]

The young Muller attended Morris High School in the Bronx while commuting from upper Yorkville in Manhattan. He excelled in school and received a Cooper-Hewitt scholarship to attend Columbia University. His father died when young Muller was 10 years old, and the family lived on a modest income from the partnership with his father's brother. During his college years, young Muller had to work odd jobs part-time to help support his mother and sister. At Columbia, Muller received his B.A. in 1911 and Ph.D. in 1916.

He knew he wanted to be a scientist and had considered engineering and basic science as possibilities when he entered Columbia. He quickly chose the life sciences after taking courses with Edmund Beecher Wilson. Morgan at the time had not yet established himself as a geneticist and Muller's only course with Morgan did not mention his work on fruit flies.[4] Muller felt intellectually excited by Wilson's ideas on

the cell and the chromosomes. He felt Morgan was muddled in his thinking on evolution and genetics. This surprising evaluation makes more sense to those who know that at the time when Muller was an undergraduate, Morgan was strongly influenced by the ideas and work of Hugo DeVries, one of Mendel's rediscoverers and the proponent of the mutation theory.[5] This theory believed new species arose *de novo* rather than by a gradual Darwinian change over hundreds or thousands of generations. Muller was a committed Darwinian and strongly supported natural selection as the basic mechanism of evolution, a view under academic attack in the early years of the 20th century.

While Muller was completing his bachelor's degree, he met Bridges and Sturtevant, who had a very different experience with Morgan. Bridges, an orphan, was benefited by a part-time job as a bottle washer and food preparer for an organism Morgan had been studying for two or three years on recommendation of William Ernest Castle at Harvard. Morgan was hoping to find new species of fruit flies just as DeVries found new species in the evening primrose, *Oenothera lamarckiana*. Sturtevant, who lived with his brother's family (he was a professor of linguistics at Columbia), impressed Morgan with his brilliance in class and with his initiative to write a paper on coat color inheritance in horses. Both Bridges and Sturtevant discussed Morgan's recent finding of a mutation (white eyes) and its unusual mode of inheritance. Muller, who shared an enthusiasm for biology through the university's biology club, was eager to join Morgan's laboratory after his graduation (he was working on a master's degree in nerve physiology at Cornell). Despite Muller's personality, Morgan took him on. Muller had a reputation for his own brilliance, especially in coming up with powerful interpretations of the new findings from Morgan's laboratory.

While a sibling rivalry simmered among the three graduate students, and Muller often was shunted to another room (to work with his lifelong friend and fellow high school alumnus, Edgar Altenburg, who was not accepted into Morgan's laboratory), these budding geneticists engaged in numerous debates and discussions of all their experimental work.[6] This makes the source of the ideas for their experiments and interpretations of the experiments difficult, if not impossible, to separate. It led to many disputes over priorities in their later careers, and a mutual hurt, each thinking the other greedy or unkind. Muller lamented that so much of his time that should have gone into carrying out the experiments of his ideas had to wait or was taken over by his rivals, because he was not supported by Morgan and he had to teach English to immigrants or work as a runner in Wall Street to earn money for his own and his mother's needs. Sturtevant did not hesitate to lament that Muller had a "priority complex" and did not credit others for their own insights. Morgan sided with Sturtevant and Bridges; he took the view that ideas were cheap and commonplace and of little importance without the experiments to test them. It was Morgan who chose his own title, professor of experimental zoology. Morgan never felt embarrassed with his wrong ideas (he had many) because they fell by the wayside when he put them to test.

Although Muller finished his dissertation work in 1915, his degree was not awarded until 1916. His dissertation was on crossing over, a phenomenon first discovered in England and misinterpreted by Bateson as coupling and repulsion.[7] Bateson thought of Mendelian units almost like bipolar magnets that repelled or attracted each other. A different model impressed Morgan, one that stemmed from his reading of a paper by F. A. Janssens on meiosis, which showed chromosomes twisted around each other. Morgan speculated that

these twisted threads could break and reunite, separating or bringing together segments of a paternal and maternal homologue. He called the process "crossing over."

Sturtevant used the data from Morgan's first X-linked mutations and constructed a map. Muller was in awe of Sturtevant's interpretation. (Sturtevant was still an undergraduate when he created the first map). Muller suggested using the ratio of crossovers to the total of crossovers and noncrossovers for determining the map unit. (Sturtevant had used the ratio of crossovers to noncrossovers). Muller then followed up the mapping of the mutations and determined that genes kept in heterozygous state for several generations did not lose their specificity. He also worked out a mechanism and interpretation, measured by what he called the coincidence and interference of crossing over for inconsistencies in map length. This resolved the observation that certain linked genes (those relatively close to one another) had a predictable distance when their individual internal distances were added, but those relatively far apart fell short of that predicted distance. In Muller's interpretation, genes close together rarely had intervening double crossovers and those farther apart usually did. This made the longer distances shorter than the sum of the distances of contiguous segments within that stretch between the two outer genes. Muller believed the first break led to a release of tension nearby and this prevented multiple crossovers in that region.

## GENETICS AT RICE UNIVERSITY

Muller decided to leave Morgan's laboratory after a visit by Julian Huxley, who had been appointed as the founding chair of the Biology Department at the new Rice Institute. Huxley was impressed by the work of the Morgan school, and he asked Morgan to recommend a student; he recommended Muller for the job. Muller established a lifelong

friendship with Huxley in those few years they had together at Houston. It made each a strong supporter of the genetic mechanism involved in the Darwinian natural selection. By 1917, however, Huxley felt compelled to return to England to enlist in the war. He left Muller in charge and Muller hired Edgar Altenburg to share the teaching while they carried out research on mutation rates and the mutation process. Muller also continued with Altenburg a long-term project started in 1912 that was not published until 1920: a study of what Muller called the gene-character problem.

On theoretical grounds Muller had argued that Darwinian variation has a genetic basis and there must be subtle modifier genes involved in the different expressions of a genetic trait. Morgan had found two such mutants, one called Truncate and the other called Beaded wings. In both cases the shape of the wing varied and neither stock could be made homozygous. They kept throwing off normal winged flies. Morgan had turned these over to Muller to play with and as the years went by, Muller accumulated the evidence that these were complex hereditary systems. In Beaded wings the dominant chief gene (Beaded) was made perpetually heterozygous with rare or no normal-winged flies. The stability of the heterozygote arose from Muller's determination that Beaded, while dominant for its visible effect, was recessive for a lethal trait. In the homozygous state it killed the embryo. In one line of Beaded a second recessive lethal arose, but it arose in a homologous chromosome, rendering the unrelated lethal perpetually heterozygous. This new lethal was stabilized by a repressor of crossing over (then called a C factor and later recognized as a chromosomal rearrangement, an inversion) (1918).

The analysis of Truncate wings (jointly done with Altenburg) was even more complex, with isolated and mapped modifier genes, which Muller called intensifiers and dimin-

ishers, affecting the expression of the dominant chief gene (1920,1). (Like Beaded, Truncate was a recessive lethal and dominant visible mutation.) There were also environmental modifiers, especially temperature: the mutant expression enhanced at higher temperatures and the normal phenotype at the lower temperature. Muller considered these experiments of supreme importance for the emerging neo-Darwinism, which attempted to bring classical genetics into Darwinian natural selection. In nature, he argued, genes evolve through systems of modifier genes that eventually become homozygous and stabilize the new trait. He also used his analysis to discredit DeVries's mutation theory. Muller argued that the new species DeVries obtained in *Oenothera* were actually complexes of chromosomal rearrangements that underwent occasional crossing over, chromosome doublings, or losses of chromosomes, leading to the expression of many changes in the plant's phenotype and rendering it incapable of breeding with the original type. *Oenothera*, he argued, was an aberrant mechanism of evolution and not in the Darwinian mainstream.

Muller's views, initially formulated in the debates with students in the biology club at Columbia, were initially based on theoretical considerations, and he clashed in print with Castle over Castle's interpretation of hooded rats and other variable traits in small mammals (1914). Castle argued that the genes themselves varied through contamination in the heterozygous state, a claim Muller challenged in his own dissertation work and that he could now demolish with the clear evidence of modifier genes and a reductionist explanation of DeVries's own competitive model of evolution. For Muller the gene was stable until it was itself mutated and that mutation rate, as he and Altenburg demonstrated, was relatively rare.

Muller left Rice to serve as an interim professor at Columbia while Morgan was away on sabbatical leave. Muller hoped to join the faculty there but Wilson felt it would not work out if Morgan came back, which he did for a few years before leaving to head and develop the new Department of Biology at California Institute of Technology. While at Columbia (1919-1921), Muller published several theoretical papers that charted a future course for his research (1920,2; 1921,1,2; 1926). He argued that mutation should be limited to changes in the individual gene and that they should not be lumped together with other hereditary changes such as nondisjunction, polyploidy, and chromosome rearrangements. He also believed genes should be analyzed through their mutations. He considered the gene as having a unique property in replicating its variations and that something basic was present in the gene, which made it unique to all life forms. He also recognized a similarity between genes and viruses, comparing viruses with "naked genes." He believed the gene would someday be accessible to chemical and physical analysis.

## GENETICS AT THE UNIVERSITY OF TEXAS

Muller returned to Texas but not to Rice. Instead he chose a position at the University of Texas at Austin. He had a powerful influence on his colleagues, especially John Thomas Patterson and Theophilus S. Painter. Patterson was studying armadillo embryology and Painter was working on the cytology of spiders when Muller joined the faculty. After Muller showed the versatility of *Drosophila* as a tool for genetic analysis, both Patterson and Painter switched their organism of choice and became major contributors to *Drosophila* genetics. This was both a benefit and a difficulty. It increased the stimulation of discussions and approaches to work in classical genetics, but it also led to a renewed rivalry,

with Muller feeling that much of his time and ideas were entering the work of his colleagues and his own work was suffering from neglect. He tried to solve this by working at night, not a very good idea for a married man, and soon his marriage was foundering and, of course, he had alienated Patterson and Painter.

Muller alienated his colleagues as well as the university in other ways. He became an *ex officio* adviser of the National Student League, named by the FBI as a communist student organization, and he became an underground editor of *The Spark*, a newspaper promoting socialist goals, including civil rights for African Americans, equality of opportunity for education and careers for women, unemployment insurance for the unemployed, social security for the retired, and other progressive legislation championed especially by the Communist Party, for which Muller had strong sympathies although he never joined.

It is remarkable that as Muller's personal life became more complicated with marriage to Jessie (who was fired from the faculty in Mathematics when she became pregnant) and conflicts emerged with his colleagues, he became more intensely involved in his major discovery. When he came to Texas he was hoping eventually to induce mutations. He had tried, unsuccessfully, a number of chemical approaches based on the finding that temperature increased the mutation rate in a way consistent with the Q10 of chemical reactions. In 1926 he reexamined the use of radiation. Morgan, Blakeslee, and Payne had tried radiation without success about 1910. Muller realized that a subjective search for mutations was not reliable. (Although Lewis J. Stadler used that method successfully with maize, his papers appearing several months after Muller's *Science* paper appeared [1927,1]). Instead Muller designed tools to isolate the most commonly occurring mutations, recessive lethals (first discovered by Morgan).

One of Muller's great contributions to genetics was stock design. He used complex rearrangements and combinations of recessive and dominant visible markers to identify the passage of chromosomes from parent to offspring. One such stock, called *ClB,* consisted of a recessive lethal, a crossover suppressor, and the dominant visible mutation called Bar eyes, all on the X chromosome. By irradiating normal or wild-type male flies and having the X chromosomes of their sperm individually rendered heterozygous with the *ClB* chromosome, Muller could test for the presence of an induced recessive lethal mutation by looking for the absence of that category among the progeny (the grandsons of the irradiated male). This gave Muller a quantitative measure of induced mutations, and he was surprised and elated by an abundance of induced mutations that were 150 times more plentiful than spontaneously arising mutations. He not only obtained the lethal mutations he expected but also visible mutations that were both new and allelic to spontaneous forms previously picked up over the prior 15 years in laboratories around the world.

Muller published his results (without data) in *Science* (1927,1) to establish his priority and that same year presented the data in great detail at the International Congress of Genetics in Berlin (1927,2). The publicity for Muller's report of artificially induced mutations was worldwide and Muller returned to the United States with international stature. The Berlin paper mapped the lethals and visible mutations, eliminated competitive models of genes as bean bags of particles, and revealed that a portion of the first generation of mutations was fractional or mosaic (a condition associated with the DNA double helix model and not successfully interpreted until the 1950s).

## PERSONAL SUCCESS AND FAILURE AT TEXAS

Muller's troubles at Texas intensified, as he and Jessie considered separation and Patterson and Muller were no longer on speaking terms. Muller had also intensified his left-wing behavior by bringing two Soviet students to his laboratory, Solomon Levit and Isador Agol, on Rockefeller scholarships. Levit collaborated with Muller on human genetics, a field that Muller felt needed some basic science to improve its study of human traits. Muller had published a paper (1925) on identical twins raised apart arguing that very little was known of the genes involved in human behavioral traits and how they interacted with the environmental factors. He did believe such analysis, like his earlier work with Beaded and Truncate, was eventually feasible, and identical twins was one way to start.

In 1932 Muller's personal life began to collapse over his marriage, his discontent with Texas, the investigations of the FBI, veiled references to him in the local newspapers as a communist subversive on campus, and claims Stadler and others were making that X rays did not induce gene mutations (as changes in the individual gene) but instead induced chromosome rearrangements of various kinds and sizes. Muller disappeared from his laboratory and did not show up to class, and after his wife called anxious about his whereabouts, a search posse of faculty and graduate students went looking for him in the woods near the outskirts of Austin. He was found walking, muddied, and wrinkled by an overnight rain, and somewhat confused. He had slept off an overdose of barbiturates in a suicide attempt but returned to his class the next day as if nothing had changed.

The suicide attempt occurred just before he left to make presentations at the Third International Congress of Eugenics at the American Museum of Natural History in New York City and at the Sixth International Congress of Genetics in

Ithaca at Cornell University. To the amazement of many who knew him, both were major papers that had significant impact on those who heard them. At the eugenics congress Muller presented "The Dominance of Economics over Eugenics" (1932,1). Although C. B. Davenport had attempted to block presentation of the paper, Muller prevailed in his denunciation of the American eugenics movement.

Muller argued that only in a socialist country, where all children, male and female, white and black, had equal opportunities for education, housing, and other social services, would there be an opportunity for a successful eugenics program. American eugenics, he argued, was based on the false premises that social traits such as pauperism, vagrancy, feeblemindedness, and recidivist crime were largely innate traits. Muller argued that this was unproven and probably false. It was a shock to readers of the *New York Times* (and newspapers around the world) to hear an appeal for the end to racial discrimination, to class-based claims of inferiority, and to the oppression of women. Muller's phrasing was Marxist and his sympathies with the Soviet Union as the only country where that potential existed (so he believed) was considered both outrageous and reckless for a professor from Texas.

At the Ithaca congress Muller presented a lengthy paper (1932,2), "Further Studies on the Nature of Gene Mutation," on what might be considered a capstone of classical genetics. Muller presented a theory of gene function in which he introduced the terms "hypomorph" (less than normal activity), "amorph" (no activity at all of normal function), and "neomorph" (brand-new traits that have no counterpart in their normal allelic source). Alleles like apricot or eosin in the white-eyed series were hypomorphs; white itself was an amorph; and the Bar mutation was a neomorph. Muller demonstrated these functions using deleted X chromosomes carrying extra doses of the gene being studied.

Muller also introduced a second discovery. He used fragments of X chromosomes to identify a special category of modifier genes that he called dosage compensators to explain a phenomenon he called dosage compensation in which most genes on the X produce the same outcome quantitatively and qualitatively for gene action whether present in two doses in the homozygous female or one dose in the hemizygous male. Many of those who heard Muller's presentations were stunned by his originality, his forcefulness in presenting his views, and the importance of what he presented. Others, aware of the rumors surrounding his mental collapse and suicide attempt, found the presentations so incomprehensible and incoherent that they could not take in the importance of what he presented.

Muller returned to pack up and leave for Berlin. He had been awarded a Guggenheim Fellowship to study at the Institute for Brain Research, part of the Kaiser Wilhelm institutes. There he collaborated with N. V. Timofeef-Ressovsky in studies on target theory and the expression of partial dominance by recessive lethals. He arrived in 1932 but the following year Adolf Hitler was elected chancellor and the institute was vandalized by Nazis, who looked with suspicion on the communist leanings of that unit. Muller left to accept an invitation from N. I. Vavilov to come to the Soviet Union and establish a genetics laboratory in Leningrad. At the time, Vavilov's position was similar to that of the secretary of agriculture in an American president's cabinet.

Muller's five years in the Soviet Union (1932-1936) were transforming. He had the best support for his research as corresponding member of the U.S.S.R. Academy of Sciences. He was also free of teaching duties. He built a laboratory first at Leningrad and then at Moscow, where he recruited several graduate students and research associates. The projects he initiated focused on gene function explored through

position effect; gene evolution studied through the Bar case; and gene structure analyzed through what he called the left-right test.

In the first of these he noted that certain genes, like scute 19, could be shifted to another chromosome and still retain the original function. Other genes in the region of the tip of the X chromosome, when juxtaposed against heterochromatin showed classical position effect variegation or loss of function (1935). The genes themselves, as his students showed, could be isolated by crossovers and restored to normal function. In the Bar case Muller made use of Painter's discovery of salivary gland chromosomes (a discovery Muller considered so important that he nominated Painter for election to the National Academy of Sciences despite his personality clashes with him back at Texas (1936,1)).

With Alexandra Prokofyeva as his cytologist in the second project Muller showed that the Bar mutation was actually a duplication and he interpreted this as a primary unequal crossover. Once established, Bar tended to revert to normal or produce a triplication, called ultraBar. Muller called this secondary unequal crossing over. The first event Muller associated with extension of individual or small numbers of genes into chromosomes and genomes in the evolution of life from the first gene, and he modified the cell doctrine with what could be called a gene doctrine, which asserts that all genes arise from preexisting genes. Muller's insight into gene evolution was amply confirmed by the nests of duplicated genes associated with the human hemoglobin A and hemoglobin B genes, each a consequence of extensions by unequal crossing over.

In the third of these projects Muller used independent inversions with breaks, one near the scute region, and the other toward the centromere heterochromatin. These heterozygous inversions provided opportunities to combine

the fragments of the yellow-achaete-scute region near the distal tip of the long arm of X chromosome. Muller's analysis revealed discrete breakage regions between genes, as if there were some inert or nonfunctional material between individual genes (1940).

Muller had ambitious plans for analysis of the gene through radiation-induced mutations and cytological studies. He also was consultant with Levit for the first medical genetics research laboratory. This was constructed in Moscow and included dozens of identical twins that were studied for their physical traits, susceptibility to tuberculosis and other diseases, behavioral responses to mechanical tasks, and similar studies that attempted to sort genetic from environmental factors. The institute published a journal of human genetics (four issues were produced). Muller looked on this pioneering effort as a prelude for his own eugenic ideals. He went ahead with the publication of a book he had started in 1919, which he called *Out of the Night* (1936,2). He asked Levit's advice on how a eugenics program could be launched in the Soviet Union, and Levit, a party member, advised him to go to the top.

Muller had the book translated and presented to Premier Stalin with a lengthy letter advocating his utopian dream of positive eugenics in a classless society. It was the wrong time and the wrong idea. At the same time as Muller was hoping to expand his genetic and eugenic programs, a countermovement was underway in Soviet science. Trofim D. Lysenko in Odessa was offering a different view of heredity based on his plant-breeding experiments. He felt that the heredity of a species was malleable if it was shattered by a provocative environment and retrained in the desired direction. Lysenko based his theory on the work of I. V. Michurin, a Russian Luther Burbank, who like Burbank believed Lamarckian transformations by the environment were assimilated by the

plants he studied. Michurin's work was primarily in fruit trees and based on grafting experiments. Lysenko's work was primarily based on changes in cereal crops, with claims that cold shocks (vernalization) could transform winter into spring wheat or even wheat into rye or oats. Lysenko and his supporters extended their theories to all of heredity, and looked upon western genetics or Mendelism-Weismannism-Morganism as an imported bourgeois capitalist, pseudoscientific system intended to check progress, support racism, and promote fascism.

A bitter debate emerged, with growing support for the Lysenkoists, who successfully lobbied to prevent the 1937 International Congress of Genetics from being held in Moscow. Muller was drawn into the controversy, complicated by the 1936 purge that Stalin had begun through assassinations, arrests, staged trials, and imprisonments of those he considered untrustworthy. Both Agol and Levit were arrested, charged with being Trotskyites, and executed. Muller debated Lysenko in Moscow in December 1936, accusing him of practicing the equivalent of shamanism instead of science and called him a fraud. Muller was shouted down in the uproar at this mass meeting of 3,000 geneticists and collective farmers, about equally divided in their support for genetics or Lysenkoism. Muller realized there was little hope for continued research in the Soviet Union, and Vavilov advised him to find a safe way out. Muller chose to enlist as a volunteer in the Spanish Civil War and he joined the International Brigade, serving with the Canadian physician Norman Bethune doing physiological research on blood transfusion.

## THE EDINBURGH YEARS

Muller stayed in Spain through the siege of Madrid and when the cause of the Republican Army seemed on the verge of defeat, he tried to find a place to go. He could not return to the Soviet Union, where he would be subject to intimidation, arrest, or execution. He could not return to Austin because he received notice that he would first have to stand trial in the faculty senate for violating a university policy as an editor of an unauthorized newspaper (university policy required signed editorials and columns on student publications). Muller hoped to find work in Paris with Joliot Curie or in Stockholm with Gunnar Lundberg, but they had no openings. Huxley heard of his difficulties and contacted F. A. E. Crew, the director of the Institute for Animal Genetics at the University of Edinburgh.

Crew arranged for Muller to be a guest investigator and Muller found himself once more with an opportunity to develop a graduate program. He arrived in 1937 and he quickly began research with some new problems to examine. He looked at the relation of radiation dose to mutation frequency and with S. P. Ray-Chaudhuri demonstrated that the same amount of mutation is produced by a given dose whether that dose is administered over a month (a protracted dose) or over 30 minutes (an acute dose) (1939). This led Muller to argue that even diagnostic doses of radiation were of concern for radiation protection and he advised practitioners of the danger possible in his annual report to the granting agency that supported his research. Physicians objected that Muller's views were injurious to patient confidence and inappropriate because the work was done on fruit flies and not human patients. It was the beginning of a skirmish on radiation safety that would persist for the rest of Muller's life.

Muller had two additional students whose collaboration proved fruitful. With Guido Pontecorvo, Muller worked

out ways to use triploid *D. melanogaster* females and heavily irradiated *D. simulans* males to construct diploid surviving embryos that carried all *D. melanogaster* chromosomes except for a fourth chromosome from *D. simulans*. The analysis of these flies allowed Muller and Pontecorvo to argue that interspecific hybrids that fail to survive owe their failure to assignable genetic differences rather than to some vague mixing of incompatible cytoplasm. Muller and Pontecorvo also used irradiation and triploid flies to identify the mechanism of dominant lethals. These were aborted embryos produced by radiation exposure of sperm (1942), and Muller and Pontecorvo showed (independently of Barbara McClintock's work on maize) that dicentric chromosome formation (what McClintock called the breakage-fusion-bridge cycle) was the source of cell death leading to the aborted embryos.

The second student, Charlotte Auerbach, like Pontecorvo was a refugee from fascism. Crew assigned her to Muller. Muller suggested to her that a productive way to study the gene was through mutation and he recommended looking at chemical mutagenesis. Auerbach used pharmacologist Robson's suggestion to use mustard gas and the first demonstration of a potent chemical mutagen was successfully published (but had to wait until the end of the war because of secrecy laws imposed on agents that were used or could be used for warfare). Also at Edinburgh, Muller met and married his second wife, Thea (Dorothea Kantorowicz). Muller had the frustrating duty of being a leading planner of the aborted Congress of Genetics in Moscow and the transferred congress that met in Edinburgh on the eve of World War II. The outbreak of war put an end to basic research in Great Britain, as a fight for survival dominated all other issues. Muller was advised to move back to the United States.

The best Muller could salvage was an interim position at Amherst College. He did not have the financial support for

research, and it was difficult to find assistants willing to work in jobs that were unrelated to the war effort. It was also a time for happiness and rediscovering family life with the birth of his second child, Helen. Muller's major activities at Amherst were writing review articles. He also worked as a consultant on radiation genetics projects for the then-secret Manhattan Project, but those could not be published. It also meant a return to teaching but Muller's heart wasn't in teaching undergraduates. As the war came to an end Muller knew he would not be added to the faculty. He wrote in desperation to friends. McClintock said a letter to her was so alarming in his despair about continuing in academic life that she burned it. Fortunately, Indiana University heard of Muller's difficulties. Fernandus Payne, who admired Muller's work, sent Tracy Sonneborn to a meeting to explore Muller's interest in joining the staff. Muller was delighted, and in 1945 he moved his family to Bloomington.

## THE INDIANA YEARS

Muller spent his happiest years in Bloomington. He felt warmly appreciated by his colleagues. He was generously supported by the Rockefeller Foundation and by Indiana University with grants to begin another graduate program. He taught at the graduate level (three courses a year), and he felt vigorous at the age of 55. In 1946 he was awarded the Nobel Prize, and that had a transforming effect on his position in the university and in national life. It was the third nomination for Muller. The rule of three prevented Muller (as well as Sturtevant and Bridges) from receiving the Nobel with Morgan in 1933. Lancelot Hogben was asked to write a nomination for Muller in 1939, but war broke out and Muller's candidacy was deferred. The bombings of Hiroshima and Nagasaki had changed the relation of science to society. An Atomic Age required public debate and Muller's prize

was seen as a message to him and to science to steer society through potential abuse or calamity.

While Muller wore the mantle of elder statesman for science, he was also committed to his graduate program. He studied a variety of projects in radiation genetics using neutrons and other particles, often in collaboration with facilities at Brookhaven National Laboratory. He also looked at new problems in human genetics. He shifted from twin studies as a tool to understanding and reexamined the survival of genes in populations. He made use of his Soviet-period research on the partial dominance of recessive lethals (work done with Kerkis) and extended it to population genetics, using a modification of equations first used by Danforth. Muller presented a new concept that he called genetic load (1950). He believed that spontaneous mutations accumulated in populations and reached an equilibrium with the amount of newly arising mutations matching those eliminated through their partial dominance. In human populations, he argued, the mutational load increases each generation because the pressure of natural selection is relaxed in an unnatural environment.

Muller and his students studied spontaneous mutation rates and used protracted and acute doses under varied physiological conditions (nitrogen- or oxygen-rich atmospheres) that might diminish or enhance chromosome breakage or gene mutation. He refined the tools for genetics and launched numerous stocks to improve the detection of lethal mutations (recessive and autosomal), sterility mutations, and visible mutations.

Throughout those years he was also embroiled in Cold War conflicts. He spoke out against radiation abuses. He was distrusted by those who misinterpreted Muller's concerns about radiation hazards in medicine, industry, and weapons testing as attacks on national defense and the survival

of the West against Stalinist imperialism. He went public on the Lysenko affair after 1948 with an attack on Soviet genetics. At the International Genetics Congress in Stockholm the eastern bloc delegates walked out when Muller started listing the crimes against science he had witnessed in the Soviet Union. Muller was called to testify before the House Un-American Activities Committee. (That testimony is still immune from access). It was an era of fear. He and his wife burned thousands of items they had accumulated in his travels, including correspondence with known communists or communist sympathizers. He hoped to protect his students and colleagues, who like him erred in thinking that the Soviet experiment was democratic and just and free of prejudice.

Muller tried to separate the politics of the Cold War from the very real issues that he felt had to be addressed. What should the maximum exposure doses be for a lifetime of medical diagnosis? How should standards be set for maximum permissible doses into the environment or in the workplace for the nuclear power plants industries were planning? When should scientists support efforts to ban atmospheric and oceanic testing of nuclear weapons? Muller's views were complex and often misconstrued. He wanted both atomic and hydrogen bombs to be developed. He felt nuclear disarmament was not possible unless it was by mutual agreement in treaties with guaranteed scientific inspection to prevent cheating. He argued that fallout doses (except for the largest of the hydrogen bombs used) were too small to be a public health threat. He argued that diagnostic doses were individually low risk, but when given to hundreds of millions of people, did induce a predictable number of leukemias, solid cancers, and mutations. He argued that the Atomic Bomb Casualty Commission in Hiroshima and Nagasaki would find few mutations in the children of the exposed population because

most mutations are recessive and they would not show up for many generations to come. Muller's views were often rejected by those who feared any dose of radiation however small and by those who dismissed low doses as harmless or even beneficial to the public (because they allegedly created a hybrid vigor in the offspring).

In 1957 Muller revived his eugenic ideals (1959, 1961). He felt the abuses of Nazi eugenics and the American eugenics movement were historical accidents not likely to be repeated in democratic societies. He urged in such societies the adoption of his idea, germinal choice, which should give to the user the decision making on what sperm or eggs to use for producing children. He hoped people would learn to separate sexual activity from the quality of children they desired, just as they had learned to separate sexual activity from reproduction by the adoption of artificial means of birth control. In addition to family planning based on thoughtful desires for children, he recommended a genetic enlightenment that would be most likely to produce healthier, wiser, and more caring offspring. He was criticized in editorials as being ignorant of the Holocaust and the excesses humans are cable of applying against humanity. Many thought he was trying to revive the old-line eugenics he had condemned. Muller realized as his health began to fail that no eugenics was better than bad eugenics, and he refused to endorse a planned sperm bank in California for germinal choice that was based on the values of old-line eugenics.

## MULLER'S LEGACY

Muller led a flawed life. His political involvement in the uses of genetic knowledge made him vulnerable to controversy and negative assessment. It is difficult to speak out on important issues without experiencing rejection or being misconstrued. He told his students that it was their duty to

bear witness and to speak out against the abuses of science in their generation. Most scientists have difficulty playing the role of a gadfly. They enjoy doing their science and not worrying about the way their findings will be used. Muller was not alone in taking public stands. Julian Huxley, J. B. S. Haldane, Linus Pauling, Joshua Lederberg, and James Watson are among the many scientists of stature who have spoken out against public policies that seemed injurious to the public. He argued that genetics was the most subversive science because it dealt with issues fundamental to human nature. A geneticist cannot expect to be ignored by those who reject natural selection and evolution. Geneticists are bound to encounter public controversies as their findings are applied to human reproduction. At worst, the government, as in the Soviet Union or in Nazi Germany, may endorse a spurious science to counter the findings developed by geneticists. Muller's views on eugenics are complex. In the long run he may turn out to be prophetic and genetic-load concerns in distant generations may lead to germinal-choice reproductive options to reduce that load. Muller served humanity well in promoting radiation safety and helping to curb the most egregious abuses of radiation in industry and health.

Muller's roles in contributing to classical genetics, in founding the field of radiation genetics, and in relating genetics to evolution are solid contributions that will endure. His influence on the careers of many of his colleagues and those who took his courses was profound. He had some successful students, including Bentley Glass, who was elected to the National Academy of Sciences. Both Pontecorvo and Auerbach became fellows of the Royal Society. Many of his students entered academic life and had productive careers. Many of his students in the Soviet Union were not so fortunate, and they spent years isolated from publishing, forced out of genetics, imprisoned, or executed. It is a tribute to

Fernandus Payne that he recruited Muller. Payne dismissed the claims of psychosis, communism, and a personality likely to be disruptive to colleagues. Muller had his difficult moments at Indiana but more often than not he brought glory to the university; he respected his colleagues (refusing to teach less than they); and he deeply appreciated the gift of tranquility bestowed on him. Those students who worked with him will appreciate his kindness in encouraging their careers, helping them financially through hard times, and fighting passionately with them on every sentence they wrote in their articles with the conviction that what they did mattered and deserved the tough evaluation of his considerable knowledge.

## HONORS AND DISTINCTIONS

In addition to his Ph.D. in 1916 at Columbia University, Muller was the recipient of five honorary degrees: D. Sc., University of Edinburgh (1940); D.Sc., Columbia University (1949); D.Sc., University of Chicago (1959); M.D., Jefferson Medical College (1963); and Ph.D., Swarthmore College (1964). He received numerous prizes and recognitions of his stature in his career: the Cleveland Research Prize, American Association for the Advancement of Science (1967); Nobel Prize in Physiology or Medicine (1946); president, VIII International Congress of Genetics, Stockholm (1948); Kimber Award in Genetics, National Academy of Sciences (1955); Virchow Medal, Virchow Society of New York (1956); vice president, International Congress of Radiation Research, Burlington, Vermont (1958); Darwin Medal, Linnaean Society, London (1958); Darwin Medal, Deutsche Akademie Naturforscher Leopoldina (1959); Alexander Hamilton Award, Columbia University (1960); Humanist of the Year, American Humanist Association (1963); and City of Hope Medical Center Research Citation (1964).

Muller was a member of numerous learned societies in the United States, including the National Academy of Sciences (elected in 1931); fellow, American Association for the Advancement of Science; American Society of Naturalists (president, 1943); American Philosophical Society; American Academy of Arts and Sciences; American Society of Zoologists; Genetics Society of America (president, 1947); American Genetic Association (vice president, 1959); Society for the Study of Evolution (president, 1957); American Society of Human Genetics (president, 1949); Society for Experimental Biology and Medicine; American Humanist Association (president, 1956-1959); honorary member, American Institute of Biological Science.

Muller was also elected to the following foreign learned societies: the Royal Society, London; U.S.S.R. Academy of Sciences, corresponding member (1933, resigned 1948); Royal Danish Academy; Royal Society of Edinburgh; Royal Swedish Academy; Accademia Nazionale dei Lincei; National Institutes of Sciences of India; Akademie der Wissenschaften und Literatur, Mainz; Genetics Society, Japan; Genetical Society; Mendelian Society of Lund; Deutsche Akademie Naturforscher Leopoldina; Japan Academy; Zoological Society, Calcutta; Societa Italiana di Genetica Agraria; Rationalist Press Association; World Academy of Arts and Science (vice president, 1964).

## NOTES

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3. Muller's papers are mostly stored in the Lilly Library at Indiana University in Bloomington. A smaller collection of Muller correspondence and papers is stored at the archives of the Cold Spring Harbor Laboratory Library, New York.
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