H. J. Muller, Crusader for Human Betterment

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When very young, H. J. Muller became possessed by a vision of man's potential long-range future. It is the key to understanding and appreciating his life and work, for they were singularly dedicated to a crusade for implementing a start toward realization of the vision. Even during his final illness (*1*) he still conversed passionately about the same vision, the genetic and social betterment of man—of *all* men, of all colors and of all nations.

Roots

His view of the roots and development of the guiding motifs of his life are recorded in his own words in unpublished autobiographical notes (*2*):

> Herman J. Muller, senior, my father, was a strong influence in my life although he died . . . when I was only 9½ years old. . . . My father did much to imbue in me a strong sympathy . . . for oppressed peoples, and . . . the scientific view of nature: . . . the lawfulness of the working of matter, the grandeur of the story of evolution. . . . When I was about eight years old, my father took me to the American Museum of Natural History, and, as I well remember, made clear to me, through the simple example of the succession of fossil horses' feet shown there, how organs and organisms became gradually changed through the interaction of accidental variation and natural selection. . . . And from that time the idea never left the back of my head, that if this could happen in nature, men should eventually be able to control the process, even in themselves, so as greatly to improve upon their own natures.
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> In 1906 I began a lasting friendship with Edgar Altenburg, then a classmate. . . . He and I argued out vehemently and to the bitter end all questions of principle on which we differed, and thus he succeeded in converting me both to atheism . . . and to the cause of social revolution.

In 1908, at age 17, Muller read Lock's *Recent Progress in the Study of Variation, Heredity, and Evolution* (*3*) and records in his autobiographical notes:

> I became thoroughly convinced by this book of the generality of Mendelism as *the* method of heredity, of the material existence of the genes as particles lying in line in the chromosomes and exchanged between them, and of mutations of these genes as the primary steps of evolution, subject to natural selection. An inimitable course under Wilson in heredity and evolution taken in the following year [1909], and cytology the year after [1910] strengthened me in these convictions, and when . . . Morgan began getting mutations in *Drosophila* . . . I, together with some others [Altenburg, Sturtevant, Bridges], became greatly excited and eager to join in this work.
>
> In 1910–11 I had my first opportunity to do some minor experiments with the flies, and also to take Morgan's course.

Toward the end of the autobiographical notes (*2*) he wrote the following key passage:

> The original source of my interest in genetics had been my long-harbored idea of the control of the evolution of man by man himself. I had intentionally, however, devoted most of my efforts to the investigation of the general genetic basis, being convinced that this would provide a surer foundation and backing for a later attack on more specifically human problems. Only so could the necessary knowledge, as well as the authority, be obtained.

There you have the object and the strategy of his grand crusade: first, investigate basic genetics in order to obtain the needed knowledge *and authority*; and then use both the knowledge and the authority in the attack on *human* problems, including the ultimate objective, man's control of his own evolution.

Trunk

For nearly 20 years following his initiation into genetics, Muller therefore concentrated on obtaining the fundamental genetic knowledge, with the brilliant results familiar to all of us. His earliest contributions, along with those of Morgan, Sturtevant, and Bridges, were integrated into their book of 1915, *The Mechanism of Mendelian Heredity* (*4*), which marked the establishment of the chromosome and gene theories of heredity. After leaving this group the year the book was published, Muller exposed the phenomenon of balanced lethal genes and, with Altenburg (*5*), made a thorough analysis of the theoretically important case of truncate wing. As a highly variable trait, truncate symbolized the difficulty of comprehensively extending the domain of Mendelian heredity. By initiating the use of clear-cut markers for each linkage group, Altenburg and Muller exposed a system of multiple and modifying genes affecting truncate. This analysis not only extended Mendelian heredity to include such variable traits but served as a model of the way in which variable, multiple-gene, quantitative traits could be effectively studied.

Important as these contributions were, they are overshadowed by Muller's two supreme achievements of this first period of his scientific career: his chief theoretical contribution, the theory of the gene as the basis of life, and his chief discovery, the experimental production of mutations. They remain the two greatest scientific contributions of his life.

During this first period of his career, up to 1927, he published very little about applications to human problems. In the paper on truncate wing (*5*) the possibility of studying human psychological traits by the marker method was pointed out, and the use of blood antigens as potentially good markers was suggested. Toward the end of a paper on mutations (*6*), Muller asked, "Are there any applications of the knowledge which has already been gained about mutation in general, to eugenics and to the principles which should govern us in guiding human reproduction?" And he answered, "I think that one such application is already clearly indicated. . . . It is . . . necessary for man . . . to resort to a periodically repeated, although not continuous, series of inbreedings and selections . . . to . . . prevent . . .

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spontaneous deterioration with complete and permanent collapse of the evolutionary process." This was the first of Muller's many comments on the problem of man's load of lethal and detrimental genes.

Two years later, Muller published his famous study (*7*) on a pair of identical human twins who had early been separated and reared apart under considerably different circumstances. The exploitation of early separation was both an all-important advance over Galton's 19th-century studies of twins and an approach to the problem of the genetics of human psychological traits which could be pursued while waiting for discovery of the marker genes required for more precise analysis. Muller used the twin data to show the interaction of genic and environmental factors in human psychological traits.

That is the extent of his published applications to human problems up to 1927. However, he went far beyond this in speech. While a 19-year-old undergraduate at Columbia University, when he began to work with *Drosophila* in 1910, Muller (*8*) read to a radical student club, the Peithologian Society, a paper called "Revelations of biology and their significance." I have had the privilege of reading this remarkable paper, which Muller carefully preserved, in hand-written manuscript, with the notation "very important." It foreshadows his whole subsequent career as researcher and crusader, as a few words from it will make clear:

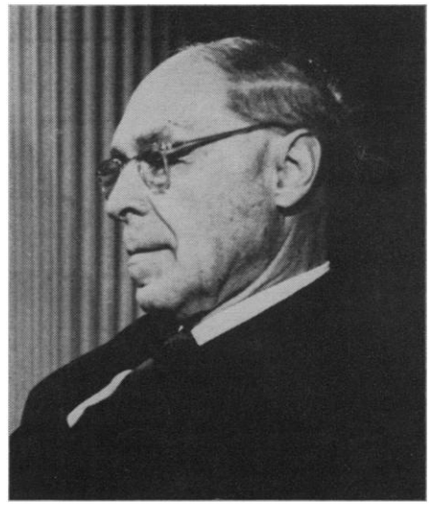
> Those will become supreme who not only care for those now living, but include, as it were, in the social organization, the remotest future, by applying the principles of heredity and variations. . . . The way to eliminate the unfit is to keep them from being born. . . . But . . . we should not only check degeneration—negatively—but further evolution, positively [by artificial insemination], and work for the production of a nobler race of beings. . . . Mankind has nothing real to lose, but only to gain, by a process of evolution. . . . With knowledge of the laws of nature comes power to manipulate them, and knowledge of life thus means the perfection of man.

The socialistic, genetic, and evolutionary prospects for man set forth in this lecture were greatly expanded in 1925 into a series of lectures delivered at the University of Chicago. They were further expanded and eventually published 10 years later as *Out of the Night* (*9*), the only book of which Muller was sole author. I return to it below in considering the next phase of his career.

Branches

The induction of mutations by x-rays at once won him the Newcomb Cleveland research prize of the American Association for the Advancement of Science and led directly, but belatedly, to the Nobel prize in 1946, nearly 20 years later. These two decades between the prizes were a period of branching out, of transitions and of crises. His success with x-rays, opening up the practical study of mutations, made it possible to branch out into varied aspects of mutation research, and he seized the opportunity. He examined internal and external factors affecting mutation rates, dosage-effect relations, dosage compensation, chromosomal aberrations, position effects, heterochromatin and inert regions, variations in degree of dominance and recessiveness, questions of gene discreteness and integrity, and the bearings of the old and new knowledge on systematics and evolution. The breadth and depth of Muller's contributions to general genetics cannot be sketched briefly. As Lederberg wrote (*10*), "It is not easy to find an original thought in biological theory that has not, in some way, been anticipated [in his papers]."

The broad range of Muller's publications now began to extend much more to specifically human problems, for he had gone far toward fulfilling his plan of first acquiring the knowledge and authority. The mutagenic action of x-rays provided him with clear new applications of genetics to man. So he began, at first with little success, his long campaign of pointing out, especially to physicians, the genetic hazards of medical and other uses of x-rays, the importance of shielding gonads, and the nature of the spread, accumulation, and delayed expression of x-ray-induced mutations.



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However, most of his publications on human problems in the period between the prizes were devoted to sociopolitical problems. His autobiographical notes tell why he had earlier considered it prudent to refrain from printing his views or even, as a rule, from expressing them in speech. He lacked the needed authority, and neither the time nor the place was propitious. After 1927 he had sufficient authority. After 1929, when the great economic depression hit the United States and many intellectuals were drifting strongly to the left, the time seemed ripe. In 1932 he left Texas for Germany, and, by late 1933, he had settled in the U.S.S.R., where he obviously would not suffer, as he had previously, for his communist sympathies.

Just before leaving the United States he addressed the 3rd International Congress of Eugenics, in New York, on "the dominance of economics over eugenics." In a footnote to this paper (*11*) he refers to his youthful unpublished speech before the Peithologian Society at Columbia (*8*) as an earlier formulation of some of the same ideas. His thesis was that, in a capitalistic, class-stratified society, the environmental condition of the masses prevented them from exhibiting and realizing their genetic potential, and the values and entrenched antiquated notions of the upper classes would inhibit the introduction of eugenic measures. As he put it, "impending radical changes in our [the United States'] economic order are prerequisite to a genuine functioning eugenics."

Two years later, his book *Out of the Night* (*9*) appeared in the United States while he was in the U.S.S.R. Also based to a considerable extent on his youthful address before the Peithologian society, *Out of the Night* is the fullest, most inspiring, and in some respects most brilliant exposition of what his life-crusade was all about. The following passage conveys its spirit.

> The biologist's view is the long view, covering aeons composed of millions of years. By the standards of the man in the street he would appear crazy. But he has the evidence, he has seen the panorama, and he *knows* that life as a whole is ceaseless change, that the accomplishments even of *natural* evolution far surpass any other type of progress that he could have imagined possible, and that there is no sign of a physical limit yet. There is no perma-

nent *status quo* in nature; all is a process of adjustment and readjustment, or else eventual failure. But man is the first being yet evolved on earth which has the power to *note* this changefulness, and, if he will, to turn it to his own advantage, to work out genetic methods, eugenic ideals, yes, to invent *new characteristics, organs,* and *biological systems* that will work out to further the interests, the happiness, the glory of the god-like beings whose meagre foreshadowings we present ailing creatures are.

Out of the Night not only set up the genetic goal but, like the paper on economic dominance, tied it to the socialist-communist revolution as essential for achieving the liberation of mind and the equality of opportunity required for effective and sound control of human evolution. The hope that this great crusade might be accomplished in the Soviet Union was dashed with the rise of Lysenko and the plight of genetics in the U.S.S.R. under Stalin. Muller recognized that the chief culprit was authoritarianism in every form. Reversing his former vigorous stands, he concluded with equal vigor that interference with intellectual freedom could be more effectively combatted in the West than in the U.S.S.R. Thenceforth he directed his social, economic, and political efforts toward correcting the evils of the West.

His first major opportunity to do this came at the 7th International Congress of Genetics at Edinburgh, Scotland, in 1939. There a "Manifesto" (*12*), signed originally by Muller and six other geneticists, was addressed to the question "How could the world's population be improved most effectively genetically?" Its thesis was that the primary need is major changes in social conditions and human attitudes—namely, changes from a capitalistic class-stratified society to a socialistic state in which biological principles become common knowledge, birth control and artificial insemination are legal, and positive selection and large-scale genetic research on man are fostered. Conspicuously absent, perhaps at the insistence of some of the signers who had not yet gone as far as Muller in the break with Lysenkoism and Stalinism, was the key thought of the need for intellectual freedom unfettered by authoritarianism. Nevertheless, the "Manifesto," which Muller lists as one of his publications, shows clearly that his disillusionment with Stalinism left completely unchanged his conviction that a socialistic economy was necessary for effective and wise control of human evolution.

Fruits

The stage for the last two decades of Muller's crusade was set by momentous global, scientific, and personal events. In 1945 the dreadful atomic age began, to be followed within a decade by the beginning of the space age. The dominant position of science and technology in the modern world became obvious to all. Allied with government, scientists and technologists received rapidly growing support, and science flourished. Even before Sputnik, the Watson-Crick revolution in genetics had begun, and it prospered greatly from the new bounty. Its sensational advances passed with amazing rapidity from the laboratory to the newspapers and magazines, sometimes before they appeared in scientific journals. DNA and the gene became household words. Meanwhile, the award to Muller in 1946 of a Nobel prize made him known to the general public as the discoverer of the mutagenic effect of irradiations.

Crowned with the prestige of this highest recognition, and taking advantage of the new public image of science and the scientist, Muller contributed mightily toward putting genetics before the public and toward guiding the public to think ahead—farther ahead and more urgently than ever before. He poured forth a torrent of speeches and publications (more than 200 in his last 20 years), about half of them addressed to nongeneticists.

At first he fought two specific battles: Lysenkoism and radiation hazards. How much effect his many attacks on Lysenkoism had either in stemming its spread to the West or in its eventual defeat in the U.S.S.R. is difficult to assess. In the end, forces within the U.S.S.R. won the victory for genetics.

In the radiation battle, the problems were intellectually less simple. Their solutions usually required weighing presumed necessities or advantages against estimated short- and long-term damage. For a decade Muller repeatedly spoke, and published, on the genetic consequences of fallout and other sources of radiation and fought for governmental honesty in presenting the facts to the public and for measures to restrict exposure to the practicable minimum. As was his usual practice, he accompanied his exposition of the general situation with specific proposals for action. He called upon physicians to cease using x-rays to stimulate or temporarily inhibit ovulation; to shield patients' gonads; to use weakly penetrating Grenz rays whenever possible; to use amplifiers and more sensitive films, so that lower doses of irradiation would suffice. He demanded that shoe stores eliminate routine fluoroscopic examinations. He advised men in general against reproduction during the two months immediately following exposure to considerable amounts of radiation. He did not fight alone. But he led the fight and doubtless had at least as large a role as anyone in its to some extent favorable outcome.

The battles of radiation mutagenesis and Lysenkoism were only a part of his grand crusade, as was his earlier and continuing battle for freedom of inquiry and criticism. His crusade was a total attack on every aspect, social and genetic, of human betterment. He worked toward a constant interplay between improvements in the gene pool and improvements in environmental conditions. He attacked with equal vigor both racists and environmentalists as being equally misguided and ultimately inimical to the advancement of man. Most of the effort of the final years of his crusade was directed toward the reform of education and the acquisition and application of genetic knowledge of man.

Muller's conception of education (*13*) called for teaching an understanding of science, the scientific view of the universe and its laws, and the scientific view of man's place in nature. He contended that the central theme must be evolution—cosmic and chemical evolution, biological evolution, and the genetic and cultural evolution of man. He believed man would come in this way to appreciate that the evolutionary advance from the origin of life to man could continue on into the future because man could direct, and thereby also enormously speed up, his own further evolution through conscious instead of natural selection.

About this great future of man, Muller was irrepressibly optimistic. He had faith that man could be motivated to subordinate his individual interests to long-range social considerations; that men could agree now on values—greater cooperativeness and higher intelligence—that would be worthwhile evolutionary goals; and that achieving these goals would automatically result in agreement on further and higher values, on and on. He was not daunted by the thought that life on earth will terminate with the cooling of the sun. Occasionally he was tempted to grasp

at straws—space travel to carry man elsewhere in the universe and the eventual possibility of counterbalancing loss of solar energy by processes of energy increase; but on the whole he simply ignored ultimate limitation or doom, holding that even only millions of years more was enough to justify the great adventure of advancing individual human life to ever higher levels of happiness, satisfaction, and accomplishment. This was the aim of education—to present these prospects as a goal and to inculcate understanding of the means of attaining them.

He set forth a vast program for attaining needed genetic knowledge of man in a paper (*14*) which launched the American Society of Human Genetics and its journal and in his address (*15*) as first president of the Society, as well as in a number of other papers. Among other things, he called for studies for obtaining marker genes and for mapping human chromosomes; for cytological studies to identify each chromosome and chromosomal aberration; for cytogenetic studies on isolated human cell and tissue cultures (that was in 1949!); for study of twins and the use of statistical methods of analyzing each specific case of gene-environment interaction; for studies of expressivity, penetrance, conditional dominance, and degrees of dominance; for studies on other animals to aid human genetics; for studies on the whole range of problems of population genetics; and especially for attacks on quantitative characters, which he always considered to be of primary human importance, since they included health, vigor, longevity, and all mental and psychological characters.

His own investigations were concentrated on the study of detrimental and incremental genes; on the ascertainment of their rates of occurrence, persistence, spread, and long-term effects; and on estimations of mutational loads. He repeatedly pointed out that the more society compensates—by hygiene, medicine, and the like—to render otherwise lethal or detrimental genic effects tolerable, the more these genes spread until they become in effect the wild type, or normal; then everyone has to have compensatory treatment. Meanwhile the same thing would happen with more and more gene loci. He saw this as an endless and cumulative process analogous to the Malthusian cul-de-sac and ending logically in the need for environmental compensation for the entire genome—a *reductio ad absurdum*. This argument, he held, meant that sooner or later we would have to take a firm genetic stand—that is, make a compensatory selection—to halt genomic decline. Seizing on evidence that so-called recessives prevailingly exhibited some degree of expression in human heterozygotes, he emphasized how this increased the value of the phenotype as a guide to selection of genotypes. Together with his calculation of the amount of selection needed merely to maintain genetic equilibrium, this bolstered his optimistic hope that it would be practicable not only to prevent increases in the mutation load but to attain some measure of success in improving man's gene pool in a reasonable time, much shorter than would otherwise be expected.

Muller did not overlook the difficulties involved in providing sound guidance—the difficulty of ascertaining which individuals carried undue numbers of undesirable genes, insufficiently balanced by specially desirable ones, and which individuals carried especially low numbers of undesirable, together with a fair proportion of desirable, genes. These difficulties, together with the question of values and the slow projected rate of improvement, he recognized, but they did not lead him to conclude that action should be delayed until the questions were answered, until the difficulties were overcome, and until more rapidly effective methods were available. His stand was always to act, to do what one could, to use *now* the limited knowledge available.

His main proposal for action now, as we all well remember from the speeches and papers (*16*) of his last several years, was what he called "germinal choice." From his first public utterance in 1910 to his last in 1966, artificial insemination was his proposed first step toward man's control of his own further evolution. With the advent of successful techniques of freezing and thawing sperm and of storing them for long periods under conditions that could protect them from the action of mutagenic agents, the possibilities of artificial insemination became greatly extended. Though Muller never ceased to fight for educational and social reform, the major battle of his last years was to promote the idea of sperm banks, where the sperm of men of outstanding accomplishment or qualities could be stored and used later for artificial fertilization. To all specific objections—insufficient knowledge, the dangers of abuse, the problems of choosing donors and recipients—to all of these, and more, he developed his answers. And in the midst of this last battle he died.

Seeds

He left us the legacy of a brilliant dreamer-activist who had never lost the idealism, energy, and vision of his earliest youth. His profound respect for the dreams of the young was shown by his fondness for Edwin Markham's line, "the lyrical dream of the boy is the kingly truth." With a singleness of purpose actively maintained for nearly 60 years, he reiterated his boyhood vision in his last speech (*16*):

> Of course we—that is, humanity—will take our biological evolution into our own hands and try to steer its direction, providing that we, humanity, survive our present crises. . . . Our genetics and our culture are inextricably interrelated. . . . The . . . important genetic problems arising out of modern cultural conditions lie in the need for a *further* advance in the genetic level of those psychological endowments which have already attained a height so distinctive of man . . . cooperativeness and general intelligence, including the creativity which arises from initiative working through intelligence. . . . We should not let ourselves be discouraged by temporary difficulties. We should not only bear in mind the urgent need for success, we should also recall that, after all, man has gone from height to height, and that he is now in a position, if only he *will*, to transcend himself intentionally and thereby proceed to elevations yet unimagined.

As we all do, Muller of course thought about individual death and like Weismann, he found it good for evolutionary reasons. He wrote (*17*): "Death is an advantage to life. Its advantage lies chiefly in giving ampler opportunities for the genes of the newer generation to have their merits tested out . . . by clearing the way for fresh starts . . ."

So, his unfinished and unfinishable task—striving to achieve man's potential for genetic and cultural advancement—becomes a challenge to those, in the generations that follow him, whose fortunate genomes and circumstances will enable them to cultivate the seeds he has strewn and planted as his legacy to the present and future. He would wish to encourage them with his favorite Markham couplet:

> In spite of the stare of the wise and the world's derision,
> Dare travel the star-blazed road, dare follow the vision.

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NEWS AND COMMENT

Budget Trauma: NSF Funds Run Dry at University of Massachusetts

Amherst, Massachusetts. Rudolf M. Schuster, professor of botany at the University of Massachusetts, felt highly honored when he was chosen to contribute to the distinguished international botanic compendium, *Die Natürlichen Pflanzenfamilien*, which he describes as "the *Encyclopedia Britannica* of the plant world." Schuster was to prepare two thick volumes on his research specialty, the small, mosslike plants known as Hepaticae. The work was to culminate some 6 years of research already completed with support from the National Science Foundation. All Schuster needed to go ahead was another NSF grant to finance further research and actual writing. He got it, along with some "frosting" in the form of a second NSF grant allowing him to visit Antarctica on work that would have contributed to the project.

But getting the grants and spending the money have proved to be entirely different matters in this melancholy budget year. Schuster got caught in a budget squeeze. The NSF told his university to curb its spending, and the university told Schuster he can't spend a single penny from his new NSF grants. This freeze, coupled with other budget stringencies in recent months, has cost Schuster the services of a postdoctoral assistant, a full-time artist, and a typist. "I'm out of business," he says. "Even if I wanted to, I couldn't complete the volumes alone. And if I don't meet the contract, the publishers will get someone else to do it. Six years of work will be down the drain."

Schuster's plight is apparently not unique, for budget cuts imposed on scientific research this year seem to have inflicted great personal and professional pain on many investigators throughout the nation. Here, at the University of Massachusetts, the wreckage seems especially visible, for Massachusetts belongs to a class of perhaps 20 or more rapidly expanding institutions that has been particularly hard hit by this year's budget stringencies.

The prime mover in bringing about the cuts was Congress, which required President Johnson to reduce his projected expenditures for fiscal year 1969, the current year, by some $6 billion. The impact on research spending was uneven. Agencies with huge, multifaceted budgets, such as the Defense Department or the Atomic Energy Commission, were able to protect their basic research budgets by making cuts in other programs. Agencies whose primary business is research, such as NSF and the National Institutes of Health, had to take a big bite out of the research community.

The chief problems here have been caused by NSF cutbacks. There are scattered complaints about restrictions imposed by other agencies, notably NIH and the National Aeronautics and Space Administration, but in most cases the investigators say they can "live with" the cutbacks. With respect to NSF cutbacks, however, Arthur C. Gentile, coordinator of research and acting graduate dean, insists that the situation at Massachusetts is "very critical"—so critical, he says, that "research conducted with Foundation funds will essentially come to a standstill." That's saying a lot in a university where 30 percent of the $7.2 million in research money awarded to the university last year came from NSF.

The budget crisis at Massachusetts stems primarily from the fact that NSF's method of imposing expenditure reductions did not take into consideration the peculiar needs of rapidly expanding institutions. After the Budget Bureau gave NSF a spending ceiling for fiscal 1969, NSF in turn assigned spending ceilings to some 500 institutions and left it up to these institutions to decide what NSF-sponsored projects on campus should be canceled or cut back so that the institution as a whole would not exceed its ceiling. Unfortunately for Massachusetts, the base from which NSF computed these institutional ceilings was the amount of NSF money spent by the institutions in fiscal 1968.

Foundation officials explained that they worked from fiscal 1968 figures because these were the only firm figures available. But university administrators here feel the formula was "unfair." They say it fell more harshly on institutions that were greatly increasing their NSF expenditures than it did on more stable institutions. The expenditure ceiling imposed on Massachusetts, for example, was $996,000. This represented a cut of about 23 percent from the previous year's spending total of almost $1.3 million, which was bad enough. But when considered as a reduction from roughly $2 million in NSF expenditures that would normally have been made in fiscal 1969, the cut amounted to a whopping 50 percent. (The $2-million estimate includes expenditures from grants already awarded by NSF, from grants that were expected to be renewed by NSF, and from new grants expected to be awarded by NSF. All figures have been supplied by the