Genetic Damage Produced by Radiation

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GENETICS seems to be the field of "natural" science that is most abused by persons with political and other special interests, in their attempts to fabricate theoretical bases for their practices, as in the cases of Hitler's racist obsessions and Stalin's Michurinism. Although these two perversions are now gradually weakening their hold, they served in their day as tools in the wreaking of untold harm. In these two situations, those of us scientists who were in or near the field concerned felt it incumbent upon ourselves to speak up in the defense of science as we knew it, even though it was certainly not the force of our own words that finally turned the tide.

And now today, even in our own country, we see certain versions—or is it perversions?—of genetics raising their heads, not primarily among geneticists, but among groups who wish to create a semblance of scientific support for some preconceived policy. The matter at issue now is that of the genetic effects of radiation (*1*). This is a subject on which I have given my only previous talks before the National Academy of Sciences, one of 27 years ago and one of 14 years ago (*2*). At the present time, in view of the grave danger to which the growing distortions of this subject may lead, it would seem to be in the spirit of the Kimber Genetics Award for this occasion to be used, not for another purely academic treatment, but for a frank discussion of the matter in relation to current affairs.

Wide circulation has recently been given to statements by certain prominent publicists, including physicians and others working on government projects, alleging that the bombings of Hiroshima and Nagasaki have left the descendant populations unharmed or, possibly, even improved. Opposed to these are other voices, calling loudly, and in some cases in a suspiciously vitriolic tone, for an end to all nuclear test explosions, on the ground that even the tests are already seriously undermining the genetic basis of all mankind. To geneticists, both of these contrary claims appear so far from the truth that they can be interpreted only as special pleadings, dictated by ulterior motives.

It is no longer a matter of doubt among scientists working in this field that radiation, of the types derived from radioactive substances or x-ray machines, does produce permanent changes, mutations, in the hereditary constitution of living things of all kinds. The most numerous and important of these changes, occurring in the individual hereditary particles, or genes, and therefore called gene mutations, arise with a frequency depending proportionately on the total dose of radiation. For instance, one-tenth of a given dose produces one-tenth of the number of gene mutations, no matter in how long or how short a time that total dose was received. Thus, no exposure is so tiny that it does not carry its corresponding mutational risk.

Inconclusiveness of Hiroshima and Nagasaki data. It is well established that the overwhelming majority of mutations (more than 99 percent) are harmful, causing some functional impairment. However, any given harmful effect is usually too small to be recognized by ordinary means, especially when it is inherited from only one parent, as is almost always the case, and when, as in any human population, it occurs in the midst of a motley throng of variant characteristics, differing from person to person, which arose as natural mutations among many generations of ancestors. For these reasons, statistics on human populations, such as those obtained at Hiroshima and Nagasaki, are ill suited for finding out whether mutations have been produced by a given exposure (*3*). This is why the group of responsible scientists who signed the official report on these investigations in Japan (*4*) stated that it had "always been doubtful whether significant findings" could be obtained by the methods there used and pointed out that the inconclusive results, although definitely positive, were at the same time "entirely consistent with what is known of the radiation genetics of a wide variety of [other] material." In other words, there could well have been as many harmful mutations produced in these human populations, but lying undetected, as experiments with other animals have shown to be produced in them by such exposure.

Each detrimental mutation, even though small in effect and lost to view in the jumble of a heterogeneous population, tends to continue from generation to generation and to hamper successive descendants, until at last it happens to tip the scales against one of its possessors, and that line of descent then dies out in consequence of the inherited disability. This involves either the premature death of the affected individual or his failure to reproduce.

A significant attack on the problem of how many mutations are produced by a given dose has required refined genetic tests, utilizing reasonably uniform biological material in precisely controlled crosses. This has meant experimenting on animals and plants. The notable recent work of W. L. Russell at Oak Ridge, on mice (*5*), shows that at least 10 times as many gene mutations are produced in them by a given dose of radiation as my coworkers and I had found to be produced at a corresponding stage in

fruit flies, which had previously been the best studied material. Since human beings are so much closer to mice than to flies in all important respects, we must take Russell's figure as a closer approximation to that for human beings than the one obtained for flies.

Working on this premise, we find that, on a conservative estimate, a dose of 200 reps (*6*), such as many Hiroshima survivors must have received, would probably have caused each of their offspring to inherit, on the average, at least one mutation produced by the exposure, in addition to the several or many natural mutations, mostly derived from long past generations. It is only wishful thinking to regard the inconclusive statistics gathered on the Hiroshima population as casting any doubt on this conclusion.

Since the numerous disabilities and deaths occasioned by the induced mutations will be spread out very thinly over a large number of generations, the over-all cost, although great, will be much too scattered and insidious to affect the population as a whole noticeably. And the individual sufferers will be unable to trace their troubles to the source. At long last, the damaged heredity must become eliminated from the race by the painful process of extinction of lines. But modern high standards of living and of medical practice tend greatly to delay this elimination.

Among fruit flies, the elimination can be much faster, because it is the usual thing for more than 100 young to die for every one that survives. Thus even after massive irradiations, repeated for generations, as in the experiments carried out by Bruce Wallace at Cold Spring Harbor, the population may recover relatively soon. In fact, it may even be benefited, by the rapid multiplication, at the expense of both the weaklings and the original type, of the extremely rare beneficial mutations that the radiation had produced. But such treatment would be ruinous to a modern human population, with its already extreme variability, its very low rate of multiplication, and its artificial hindrances to selection.

Genetic effects of test explosions. To calculate the genetic damage caused in this country by all the nuclear tests to date (including both those in the U.S.A. and those in the Pacific and the Soviet Union), we will provisionally take the U.S. Atomic Energy Commission's published estimate of 0.1 r as the average for each American. In the statement that this amount is about equal to that of a chest x-ray, it is doubtless meant that the total dose reaching the reproductive organs from all the tests is about as much as reaches the interior of the chest from one chest x-ray. This amount seems minute, but we must multiply it by 160 million, representing the population. It is curious that the product that we then obtain, 16 million "man r's," is the same as that obtained when we take 100 r, assuming this to be not far from the average dose received by all Hiroshima survivors, and multiply it by 160,000, the approximate number of those survivors. Hence, the number of harmful mutations that will be inherited by our own descendants as a result of all test explosions turns out to be not far from the number among the Japanese as a result of the Hiroshima explosion.

This number of mutations is certainly in the tens of thousands at least (our reckoning gives about 80,000 as the number present in our successor population), and it will mean, in the end, several times this number of hampered lives. Yet, far more than at Hiroshima, the effects will be so scattered, in this case not only in time but also in space and separated by many more individuals who have mutations of natural origin only, that, as a group, the effects will be completely lost to sight. That is, their connection with the radiation will not be traceable. It is, nevertheless, true that each individual casualty, although concealed, must be regarded as a significant evil, which we have no right to dismiss lightly.

On the other hand, when the effects here in question are taken in relation to the total American population (numbered in billions) of the scores of generations in which they find expression, and to the total number, much larger still, of natural mutations contained in that population, it is evident that *relatively* to these totals the damage is in this case minute. It cannot be said to involve a significant undermining of the hereditary constitution of the population as a whole, for it results in an increase of much less than 1 percent (possibly less than one one-hundredth of 1 percent) in the number of mutations contained in that population.

It is true that the AEC's figure of 0.1 r received by each of us from the tests seems to represent only the gamma radiation penetrating us from the outside. Until we are given more information on how much "soft" radiation we may be getting from fallout substances that have entered our bodies, and on its persistence, all estimates of the genetic damage must remain subject to much revision upward. Yet, unless the amount of radioactive material that we take into ourselves in this way turns out to be far greater than we have been led to suppose, our general conclusion could not be altered that, relatively to the natural mutations already present, those produced by the test explosions would form only a minute contingent.

In order to decide whether a continuance of the tests is justified, it is necessary first to admit the damage and then to weigh our estimate of it against the potential benefits to be derived from the tests or, rather, against the probable damage that would follow from the alternative policy. It is only by this kind of criterion that we can justify the use of so lethal a device as the automobile, for example. In fact, automobiles kill and maim tens of thousands of us, not over a period of hundreds of years as the test explosions will, but every single year. On the other hand, automobiles in many indirect and direct ways help to save lives as well as to bring many other benefits that outweigh the accidents.

The same kind of reasoning is necessary to justify the use of carefully controlled x-rays and radioactivity in medicine. A recent U.S. Public Health Service survey (*7*) indicates that our people are annually

receiving much more radiation in these ways than they do as a result of nuclear test explosions. A significant fraction of this radiation reaches the reproductive organs. Unfortunately, however, the majority of physicians have for 28 years closed their eyes to the genetic damage. Hence, they neglect, as a rule, to provide shields over the reproductive organs of their patients and to take other elementary precautions for limiting the exposures and keeping track of the total exposure of each patient throughout his life. These practices result in the committing of entirely unnecessary and indefensible genetic damage, far greater in its totality to date, and probably per year, than that caused by all test explosions. It is largely this reckless attitude on the part of physicians that has encouraged extremists to claim that nuclear explosions are genetically harmless or beneficial.

Weighing of alternatives. So many of the public are already aware of the genetic damage produced by radiation that their morale is weakened and their apprehensions are increased when they see that the damage is denied by prominent sponsors of our national defense. Thus the door is opened for their acceptance of the defeatist propaganda which alleges that even the tests are seriously undermining the biological integrity of mankind. In this situation, the only defensible or effective course for our democratic society is to recognize the truth, to admit the damage, and to base our case for continuance of the tests on a weighing of the alternative consequences.

I submit that we do not need to fear the results of this appeal to our better judgment. Have we no right to expect individual sacrifices when the stakes are democracy and intellectual freedom themselves? Surely there is good evidence that ruthless antagonists would long since have imposed totalitarianism on all the world if we had not pushed the development of our nuclear arms, and that in fact the development of our more conventional arms, as well as of measures for reducing our vulnerability to nuclear attack, are today no less important? Is not this procedure, even though it is fraught with direst peril and requires monumental self-control, nevertheless indispensable at this stage, before we can pass to the further stage at which both sides alike will recognize the long-term futility of this unstable equilibrium and will at last agree to the globally controlled disarmament, necessarily embracing not only nuclear, biological, and chemical arms, but also conventional arms, short of which humanity will never be safe?

It is natural that those in opposition to us should be making every effort to have nuclear arms prohibited *selectively,* for that would change the military balance greatly in their favor, in view of the fact that at present we are ahead in nuclear arms and they in conventional arms and armies. Some of the critics who demand a ban on test explosions are so silent on this point that one wonders whether they are not actually aiming at this very result. But for many of us who abhor totalitarianism this form of slavery appears to be a condition as miserable and as hopeless, if grown world-wide, as the barbarism that total war might bring. Another reason why those who sincerely desire a reduction of human suffering should not limit their demand for disarmament to the more radical mass-destruction techniques is that, today, weapons of the more traditional types have been so developed that they also, in the full-scale use occasioned by a world war, would bring about wholesale catastrophe. Our own tactics, therefore, should be to continue the development of both nuclear and other arms, as well as means of protection, while at the same time earnestly offering to join in a really balanced and controlled reduction of all kinds of armaments. If we steadfastly insist on this proposition, it is unlikely that any group will be in a position to refuse it indefinitely.

Need for perspective. If we may look forward to a time when our present international tensions have become less acute, we may anticipate that in that situation the public will be in a better mind-set for viewing the whole question of the genetic damage from radiation in a still wider perspective, based upon a fuller realization of genetic processes in general. They may then come to see that even the considerable toll of genetic deterioration that a nuclear war might bring is probably not as great as that resulting from a couple of centuries of our modern peacetime civilization.

It is probably an undervaluation to suppose that in each generation we today succeed, by means of our advanced medical, industrial, and social techniques, in saving for reproduction only half of the people who in past times would have had their lines of descent extinguished as a result of their genetic shortcomings. On the basis of this conservative premise, our population would, in the course of some eight generations (not much more than 200 years), have added to its habitual "load of mutations" (*8*) about as many more as would have arisen naturally in $\frac{1}{2} \times 8$, that is, in four generations. On a provisional estimate, this would be about the same as the number of mutations that would have been produced by the irradiation of every member of one generation with 320 r. This is a dose much greater than that received by the average Hiroshima survivor. It is not, however, as great as what would have been received by a person occupationally exposed for 25 years to radiation given at the rate that conforms to what has been officially termed the "permissible dose" (0.3 r/wk).

A mutation is bad, no matter whether its presence results from the action of a previous generation in having perpetuated one that was already in existence in consequence of natural causes, or whether it had been artificially produced by application of radiation or of mustard gas. The first of these two means of getting it represents the boomerang effect, whereby our highly developed techniques result in the visiting of more of our own biological plagues upon our descendants. The only way in which such an aftermath can be avoided is by the development of more understanding and a more socially directed motivation

among the public at large in regard to matters of genetics and reproduction.

Here again the way out requires us frankly to admit and to face the problem, in the hope that the public will not wish indefinitely to continue favoring practices that lead to its genetic deterioration. Of course, this does not mean that we should abandon modern technology—far from it. It means that, in order to enable our descendants to retain the benefits of our technology, we must match it with a higher conception of our duties to subsequent generations. According to this more advanced morality, the saving of a life does not automatically justify its production of offspring, for the chief criterion on which to base decisions in the planning of parenthood would be the welfare of the descendants themselves.

Such a revision of outlook involves the development of a new and more intelligent type of idealism in regard to genetics: one that consciously strives to bequeath to each succeeding generation as good an outfit of genes as it can manage to. It is true that we might here dispute at length the meaning of the word *good,* as it is used in this connection. However, this question also is one that must be tackled eventually. There are indications that it will be found to be by no means a hopeless question, still less a meaningless one, as some critics contend, and that even genetics, through evolution science, will have some contribution to make in regard to it. If all this comes to pass, then finally in the field of human genetics, even as in that of nuclear war, the old words of Edwin Markham may prove to have been prophetic:

> The world is a vapor,
> And only the vision is real;
> Yea, nothing can hold against Hell
> But the wingèd ideal!

References and Notes

1. This article is based on an address given before the National Academy of Sciences in Washington, D.C., 25 Apr. 1955, in acceptance of the Kimber Genetics award on the first occasion of its being granted. I wish to express again my deep appreciation to the sponsors of the Kimber Genetics award, for having provided this potent means of strengthening the morale of geneticists, and this opportunity for them publicly to air the problems and the prospects of their science. This article is contribution 590 from the Zoology Department of Indiana University. It is being published simultaneously in the *Bulletin of the Atomic Scientists.*
2. H. J. Muller, *Proc. Natl. Acad. Sci. (U.S.)* **14**, 714 (1928); *Science* **93**, 438 (1941).
3. H. J. Muller, *Science in Progress* (Yale Univ. Press, New Haven, Conn., 1951), vol. 7, p. 93; *Acta Radiol.* **41**, 5 (1954); *Am. J. Obstet. Gynecol.* **67**, 467 (1954); *Radiation Biology* (McGraw-Hill, New York, 1954), vol. 1, chaps. 7 and 8.
4. J. V. Neel *et al., Science* **118**, 537 (1953).
5. W. L. Russell, *Cold Spring Harbor Symposia Quant. Biol.* **16**, 327 (1952).
6. Roentgen equivalents, physical.
7. D. W. Moeller *et al., U.S. Public Health Repts.* **68**, 57 (1953).
8. H. J. Muller, *Am. J. Human Genet.* **2**, 111 (1950).

Role of the Sciences in Education

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THERE is no unanimity regarding the roles that the sciences should play upon the stage of education. The role must be a major one if a student is to acquire a grasp of the methods and concepts of a science sufficient to equip him to enlarge its horizon or to apply it to human welfare. Upon some of the stages, whose direction has been taken over by "general" educators, sciences are assigned only minor speaking parts. Upon others they are not allowed even to speak for themselves; their parts are taken by logicians and philosophers who claim to have psychoanalyzed them and to understand them better even than they understand themselves. Again, imposters may be thrust forward, dressed in the garb of science, by a nonscientist such as a certain professor of "science education" who advertises his actor in a veritable rhapsody, as follows (*1*).

> Where democratic interplay is permitted and interchange of ideas and content information is fostered, our best people teach science in the midst of a glowing, vibrant, pulsing atmosphere of social awareness.

It is remarkable that a teacher should feel called upon to teach "social awareness" to his students, because that is a quality in many students to which one might justly apply the remark made by a southern lady who was asked whether she could supply a traveler with a little corn pone: "Bless your heart, honey, that is the only thing we ain't got a single thing in the house but."

An occasional director would keep the sciences entirely off the stage. One of them has lamented that "we" had not seen fit long ago to "starve out" science (*2*).

Many educational institutions provide two stages, one upon which the sciences act more or less alone, another for what are called on the bill "the humanities." My first purpose is to discuss the assumptions underlying the common practice of placing "science and the humanities" thus in juxtaposition.

The term *humanities* originally signified those studies having to do with the affairs of men, as distinguished from those concerned with deity, including theology. It has subsequently been given a variety of