

DEC 28 1954

W. F. Libby, Commissioner

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C. L. Dunham, M.D., Deputy Director
Division of Biology and Medicine

LETTER DATED DECEMBER 11, 1954, FROM J. A. CAMPBELL, OBERLIN COLLEGE

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Dr. Earl L. Green of the Biology Branch has prepared the following comments on the letter from J. A. Campbell to you, December 11, 1954.

Experiments in radiation genetics have led to several assertions about the relationship of radiation dose to gene mutation frequency. These assertions are, among others:

1. High energy radiation induces gene mutations.
2. The rate of induction of mutations is proportional to the radiation dose.
3. There is no threshold for genetic effect; that is, the radiation dose need not exceed a certain specifiable minimal dose (exclusive of zero dose) to induce a mutation.
4. Successive radiation doses are cumulative in effect.

Assertions 2 and 4 are generally regarded as correct, but some geneticists hold reservations about them. For example, the rate of mutation induction may be in fact linearly related to dose, but experiments are complicated due to the inability to distinguish one-hit gene mutations from two-hit chromosomal deletions which behave exactly alike in breeding tests. An admixture of one-hit and two-hit curves in experimental data may account for nonlinear relationships sometimes observed between genetic effects and radiation doses.

As another example, there may be in fact no threshold, but genetic studies at very low dosages are difficult to execute. The statement really means that no threshold has been detected in the range of dosages used. On the other hand, in one recent scientific paper, the existence of a threshold is claimed but the interpretation is suspect on other grounds.

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On the basis of experiments in radiation genetics, it may be expected that radiation of human beings by exposure to radioactive materials in connection with atomic energy operations will produce gene mutations. The question at issue, however, is not whether genes will be induced to mutate, but whether the change in the genetic constitution of the population brought about by this means is itself a matter of concern -- good, bad, or indifferent. This view of the question brings it into the area of study, theory, and experimentation known as population genetics.

All natural living populations of plants and animals, including man, which have been adequately studied, have been shown to harbor a considerable degree of genetic variability. This is true even for those species in which there is marked uniformity in morphology and physiology. It may be argued that genetic variability is necessary for a species to evolve. Further, it may be argued that mutation is necessary in order to replenish the supply of genetic diversity which is steadily being lost through selection and other agents. But this type of argument leaves out the question of whether the newly mutated genes are "good" or "bad." ("Good" and "bad" refer to the beneficial or detrimental properties with which the genes endow the organism; the term "adaptive value" is generally preferred.) Many geneticists appear to believe that radiation induced gene mutations possess lower adaptive value than genes already present in the population. This view may be correct, but it is almost surely based upon laboratory experiments designed to detect a specific class of radiation induced mutations, namely lethal mutations whose adaptive value is zero. The fact is that we have almost no knowledge about the relative frequencies of "good" and "bad" gene mutations, largely because experiments to date have not been devised to estimate these frequencies. Furthermore, the adaptive value of a given gene is not necessarily constant. In combination with some genes, a given gene may have high adaptive value; in combination with other genes, its value may be negative or neutral. In addition, the adaptive value of a given genotype may change with changing environments.

These statements are intended to convey the idea that generalizations about the genetic effects of radiation on populations are extremely difficult to reach. A wide range of opinion is clearly admissible. This is a matter over which honest and competent men may differ. The only views that seem to be clearly not admissible are the two extremes: on one extreme that any increase in the mutation rate in man is certain to be disastrous, and on the other extreme that genetic effects of ionizing radiations are not a source of concern.

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The Atomic Energy Commission is vigorously supporting research in all phases of genetics, including population genetics. During the current fiscal year, it is expected that 10 research contracts on aspects of population genetics will be in force with various colleges, universities, and private laboratories. (No work in this field is in progress at the National Laboratories.) The XI Cold Spring Harbor Symposium on Quantitative Biology, to be held on June 6 - 14, 1955, will be devoted to POPULATION GENETICS. AEC is participating in the support of this symposium.

cc: Lt. Col. H. B. Greenberg, USA

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