Speculations on Hazards of Exposure to Radiations

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Recently attention has again been called to the serious danger of increasing the amount of deleterious mutations in the human gene-pool in the face of increasing background radiation caused by atomic energy experiments (*1, 2*), once more highlighting the existence of long-range hazards as against immediate hazards of exposure to high-energy radiations. The result of this effect on future generations 100 years, and more so 1000 years, from now would appear to be disturbingly great. Basing the conclusions on the knowledge of genetics, evolution, and biological phenomena in general, the picture is not exaggerated; if anything, it is conservative. There are several aspects, however, that have received less attention and possibly can alter the picture.

One of these aspects relates to the effect of increased background radiation on the process of evolution (*3*). The resulting increase in deleterious mutations is viewed as a threat to the forward progress of human evolution. An increase in radiation that causes an increase in the rate of mutation would certainly seem to result in an acceleration of evolution, whether it is an eventual genetic deterioration, extinction, or betterment of the species. It is this point about which there may be a question. Would increased radiation lead to genetic betterment? The answer to this question would appear to be in the affirmative. Negative conclusions are based on the following assumptions. (i) The harmful effects of deleterious genes are additive in a simple way. (ii) There is a critical mutation load (a sum-total of existing deleterious genes in a population) that cannot be exceeded without threatening the species with extinction. (iii) The species is at, or is close to, optimal genetic adjustment to its environment. (iv) Laboratory experiments that appear to give an affirmative answer to the question cannot correctly be applied to the results to be expected in the wild state.

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The harmful effects of deleterious genes are not always additive. Two different genes that are separately deleterious may be beneficial when they are present together in the same individual. The very concept of deleteriousness being additive in a simple way is subject to question (*4*). Certain deleterious recessives are not harmful in the heterozygous state, while others endow the heterozygote with slight or greater advantages over the wild type (*5*). This is a condition that may be more prevalent than is recognized. The same gene may or may not be deleterious, depending on the genome in which it appears (*5*). On a long-term basis, the back-mutation rate and the mutation to the nondeleteriousness of a harmful gene must also be considered. Then, too, the environment in which the gene is to express itself must be taken into account (*6*). A deleterious gene can possibly be neutral or even beneficial in changed environmental conditions, a factor that certainly must be reckoned with when considering long-range effects.

The validity of the concept of a critical mutation load remains to be established for man. It cannot reasonably be argued that man is at or near optimal genetic adjustment to his environment, mentally or physically. That is, he is not close to an evolutionary blind alley, and much room exists for further progress. Under these conditions, increased genetic variability can lead to an accelerated evolution along beneficial lines. Laboratory experiments in which populations of *Drosophila* were subjected to high radiation doses and then permitted to breed freely bear on this point (*6, 7*). After many generations a slight but significant improvement occurred ". . . in adaptive value arising through the action of selection on either induced or spontaneous mutations," whereas there was indication of "a decreased adaptive value resulting from chronic irradiation." The latter quotation refers to experiments in which populations of flies were irradiated generation after generation with γ-radiation as high as 2000 roentgens per generation. The nonapplicability of the results of these experiments to man cannot be argued on the ground that the flies, nicely adjusted to the natural environment, were put under artificial conditions to which they made further and rapid adjustment that is not possible in the natural environment. On the contrary, it would seem to have great applicability to the human being. The question of advisability is another matter, since the cost in decreased viability on chronic irradiation is not to be advocated for man. One cannot, in all good conscience, accept such a toll for the sake of results that would take place more slowly at a lesser price. The issue at hand, however, is not a moral one but a scientific one. Would an increase in radiation speed up evolution along beneficial lines in the human being?

This reasoning assumes the normal operation of natural selection. It can be argued that man interferes with natural selection by contributing to the survival of deleterious phenotypes through his scientific and medical knowledge. But increasingly more, his capacity in this direction rests on his ability to diminish or nullify the effect of the harmful gene, in which case the gene in question is no longer actually deleterious but merely potentially so. It is true that such measures have the effect of greatly increasing the number of carriers of the potentially harmful gene, but this would not affect the forward progress of evolution as long as means are available for the neutralization or control of the effects of the gene.

Calculations on the extent of harmful effects in the remote future of an increase in the percentage of deleterious recessive mutants ignore the great strides that biochemical genetics will probably take in the not too distant future. It is not improbable that we shall eventually know the chemical composition and physical structure of the hereditary material; the step-by-step metabolism under its control in the production of the phenotype; and how to control the replication of the gene. To a limited extent the first two of these are already known. The third—the control of the replication of the gene—is not only not possible today, but there are those who even despair of its ever being possible. This undue pessimism stems in part from the belief in the fateful finality of hereditary phenomena and from the conviction that the mutation process, because of its apparently random spontaneous nature, is beyond influence from the environment and, therefore, beyond experimental direction. A case can be made for viewing mutation rates as the orderly out-come of complex biochemical events in an internal environment that adjusts in order to remain stabilized in spite of naturally or experimentally fluctuating external environmental conditions. A more subtle approach than our present attempts must be made to reach and control these events without killing the cell or organism. It is not too much to hope that success along these lines will come sooner than the 100 or 1000 years hence when, it is said, the human race will reap, in lesser or greater measure, the results of our present-day ignorance and shortsightedness. Such success will make it possible not only to ameliorate the effects of deleterious mutations but also to direct mutations back to wild type or to the production of even more advantageous phenotypes. Exploration of the implications of such knowledge is not the burden of this paper.

The greatest cause for alarm, however, is not the magnitude of the responsibility that we face for the fate of future generations. If the human race survives its present crisis it will stand an excellent chance of forestalling or even reversing what harm, if any, we may have visited upon the future. The greatest reason for concern is the damage we may be doing to the present generations, young and old. The question of maximum tolerance dose of radiation for man has not been satisfactorily determined. There has been a downward revision of this value over the years (*8*), and it may well turn out that the value is zero; that there is "no clearly safe dosage—all high energy radiation, even of low intensity and brief duration must be considered as potentially dangerous to the exposed individual" (*9*). This would not be unexpected if radiation is a "monkey-wrench" in the biochemical "works" rather than a causative agent of orderly processes. The evidence also appears to support the view that the effects of radiation damage are cumulative (*2*). At a time when we are facing an era of expanding use of atomic energy we can ill afford to pile up cumulative harmful effects. Moreover, the survival of individuals accidentally subjected to a high radiation dose (an event of increasing probability) will depend, among other things, on the magnitude of the existing cumulative effects.

In many ways, the greatest danger from poorly controlled and unnecessary sources of radiation—experimental, diagnostic or therapeutic—is to the present living generations. The lack of sufficient knowledge of the forces unleashed, the manner of their control, the safe and adequate disposal of increasingly large amounts of radioactive waste, and the methods of counteracting the harmful effects on the organism, these and many other associated problems, as yet unsolved, all should give pause to a headlong rush into any activity that has a tendency to increase the amount of radiation to which any individual is exposed. It is a matter that concerns all of us and hence all of us should be concerned about it.

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Oscar Orias, Physiologist

Oscar Orias, one of the leading physiologists of South America and well known to many in the universities of the United States, died suddenly 4 June at the age of 49. His early training was with B. A. Houssay of Buenos Aires; later he studied with Carl J. Wiggers of Western Reserve University and Walter B. Cannon of Harvard University.

After graduation from the School of Medicine of the University of Buenos Aires in 1928, Orias began his scientific career by publishing papers on hemoglobin content of blood of Argentinian men. In 1939 in collaboration with E. Braun-Menendez, he published a monograph *Heart Sounds in Normal and Pathological Conditions,* which has become a classic in the field. *Cytology of Human Vagina* by L. C. de Allende and Orias, the section on circulation in the textbook *Human Physiology* by B. A. Houssay and associates, and a monograph on *Excitability of the Heart* by Brooks, Hoffman, Suckling, and Orias (to be published in 1955) are among his contributions. He worked in many fields, and his publications revealed his high quality as an investigator.

Orias had outstanding ability as a teacher. In 1935 he was appointed professor of physiology of the Medical School of the University of Córdoba. In 1943 he was dismissed from this chair because he signed a manifesto asking for effective democratic action and American solidarity. For a brief period he again held the professorship at Córdoba but resigned in 1946 following dismissal of Houssay from the University of Buenos Aires. His courageous actions stand as a monument to the spirit of freedom.

In 1947 Orias became director of the Instituto de Investigación Médica-Mercedes y Martin Ferreyra, a post that he held until his untimely death. The trustees of this institute released him to serve as visiting professor of physiology at the State University of New York, College of Medicine at New York City on two occasions. Thus Orias made contributions to medical education in his own country and in the United States. Those who were fortunate enough to have met him will remember his clarity of perception, his gentle sense of humor, his courtesy, and his great desire to be of service to his fellow-men.

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The word 'impossible' is not in my dictionary.—RÖNTGEN.