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Biological Effects of Radiation*

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It is a well accepted scientific fact that all forms of ionizing radiation - X-rays, cosmic rays, natural radioactivity, and the many kinds of radiation from man-made nuclear reactions - cause damage to living cells. This report summarizes some of our present knowledge about such damage, points out the extent beyond which our knowledge is not yet firm, and emphasizes the difficult choices lying ahead as we weigh the benefits against the hazards of our continuing exploitation of radiation. A great problem of the present and the future is to achieve an intelligent balance between advantage and risk. For it is a mistake to assume that, because radiation damages cells, we should never permit ourselves to be exposed to it. We cannot abandon our industrial development of nuclear reactors because of the inevitable increase in stray radiation that they produce. Diagnostic X-rays may have a value far exceeding some of the dangers they cause. And it is the very capability of radiation to kill cells that makes it useful in cancer therapy.

The biologist's contribution to the problem is to make the best possible estimates of the biological effects of radiation. This is not yet easy to do with reasonable accuracy. We cannot experiment with human subjects, and the cases of accidental or wartime exposure to high doses of radiation are fortunately still too few to be of real help to the biologist. We must therefore augment these sparse data with extrapolations from experiments on animals. As a result, our assessments of radiation damage to man are necessarily approximate, indicating orders of magnitude only.

* A talk given by Professor Lewontin at an RCRI symposium on scientific and medical problems, October 10, 1963.

All ionising radiation affects tissues and cells in essentially the same way: it alters and disrupts the molecules of living material. Since different kinds of molecules play different roles in the economy of an organism, we must consider several kinds of radiation damage. The most important effects involve cell metabolism, cancer, and mutation of genes. We shall discuss them in turn.

Radiation Damage to Cell Metabolism.

Certain molecules of the living cell are responsible for normal metabolic functions such as respiration, secretion, and resistance to infection. The effects of damage to these molecules need not be permanent; the replacement of damaged molecules is itself one of the normal metabolic functions. An increase in radiation places additional strain on the repair mechanism, but it may not produce any qualitative change in the organism. Only when the dose is very high is there a significant possibility of disrupting metabolism to the point where cells, tissues, and the organism itself may die. Thus a sudden dose in excess of 600 roentgens over the whole body will kill a man, mainly by damaging his blood-forming tissue. Such a dose cannot occur in any normal way even over a lifetime; the present average rate of radiation absorption for Americans is of the order of two-tenths roentgen per person per year.

In the absence of the danger of lethal doses, we are concerned with the effects of low radiation levels on molecular destruction and repair. The main effect appears to be an increase in the rate of aging. Experimental animals subjected to non-lethal doses of radiation die sooner than control animals, but they die of the very same range of causes. In the case of rats, the mean survival rate is lowered by chronic irradiation in excess of ten roentgens per week. Smaller doses produce no apparent life shortening; it is interesting to note that doses below one roentgen per week seem to increase the survival rate. Such an increase might be due to the mobilization of repair processes that accompanies any damage to the body. Evidence for an increase in survival rates is, however, not strong.

In looking for effects of small doses on man, we can examine relative death rates for medical specialists in different fields. The samples are still too small to be statistically significant, but the data suggest that physicians who use radiological techniques have the highest mortality rate. Much more knowledge must accumulate before we can assess the life-shortening effect on the whole population of the doses which we now normally receive or are likely to receive in an unclouded future.

Radiation and Cancer.

The second and more significant kind of damage occurs in molecules which form the control system for cell division. Healthy cells divide only at the rate necessary for repair of wounds, replacement of dead cells, and normal growth. But damaged cells can divide at an abnormally high rate, displacing normal cells and tissues. This is the phenomenon of cancer. We know beyond doubt that radiation can damage the control mechanisms and produce cancer. Radiation can also cause cancer indirectly, by damaging other body constituents which then affect the control system.

The most common cancer caused by whole body irradiation is leukemia, the fatal disease in which white blood cells multiply beyond all normal bounds. There is usually a delay between the irradiation and the appearance of detectable leukemia. The delay seems not to exceed fifteen years; in eighty per cent of all cases it is less than ten years.

It is difficult to give quantitative estimates of the rate at which low dosage induces leukemia. Most of the data come from cases of high dosage, such as the victims of the attack on Hiroshima. In extrapolating to lower doses, we do not know whether there is a threshold dose below which no leukemia at all is induced. On the most conservative view, there is no threshold, and a reasonable estimate of the leukemia rate is 5 cases per 100,000 people per roentgen absorbed. For an exposure period of 50 years and the present absorption rate of 0.2 roentgen per year, we expect 50 cases per 100,000 people.

What if weapons testing were to continue at the pre-treaty level? Radiation levels in our recent past were about equally divided between natural and man-made sources. The controllable fraction came almost entirely from diagnostic and therapeutic radiation, with fallout contributing only about ten per cent. However, should testing continue at past rates, an equilibrium would be reached in which radiation from fallout would equal that from all other man-made sources. The ultimate per capita annual dose for Americans would be 0.3 roentgen, equally divided among natural sources, medical treatment, and fallout. In the absence of a threshold, each source would induce about 25 cases of leukemia per 100,000 people.

It is important to realize that we have been talking about average doses. An individual can receive much more radiation than the average, especially in diagnostic and therapeutic treatment. The pelvic X-ray examination of a pregnant woman involves an absorption of about one roentgen. Doses in other diagnostic routines, such as preventive chest X-rays, are smaller but more frequent. Chest fluoroscopy requires doses ten times higher than X-ray film. Physicians should be extremely conservative in their use of radiation, and their sources should be always calibrated to deliver not more than the necessary doses.

Genetic Damage.

We must consider a third type of radiation effect: changes induced in genes, the hereditary determinants of living cells. Unlike the first two types of damage, genetic changes do not endanger the health of the individual receiving the radiation. Instead, they affect the lives of succeeding generations.

For understanding the effects of genetic changes, or mutations, on man, these facts are important:

1) An individual receives one set of genes from his mother and a similar set from his father. Thus each of us has a double set; we are diploid.

2) Since we are diploid for each type of gene, there are two kinds of mutation: heterozygous, in which one inherited gene is mutated while the other is normal; homozygous, in which both inherited genes are mutated.

3) Virtually all homozygous mutations are deleterious, producing disease, sterility, mental deficiency, early death, and so on.

4) There is no radiation threshold; an arbitrarily small dose can induce mutations.

Mutations are occurring at all times in any population. Some arise from natural and man-made radiation. But the vast majority are due to spontaneous errors in the duplication of genes in cell division, rather than to extrinsic forces.

Thus, in every generation, mutations are replacing normal genes in the population. If the process went on unchecked, the whole population would eventually carry nothing but mutant genes. But in fact mutations tend to disappear from the population. Their carriers leave fewer offspring than normal people. Mutant individuals tend to die young, be partly or wholly sterile, or suffer from a disease which removes them from society. And their children, if any, are themselves likely to leave fewer offspring than normal. There is consequently an equilibrium between the introduction of mutations and their elimination. At equilibrium, a constant fraction of the population carries a given genetic disorder. We call such a fraction the social burden for the particular disorder.

The effect of the mutation rate, and thus of the rate of irradiation, on a social burden depends on the type of gene. We shall consider those mutations which have some selective disadvantage both in homozygotes and in heterozygotes. For such genetic disorders, the equilibrium social burden is directly proportional to the mutation rate. And the radiation-induced mutation rate is directly proportional to the rate of irradiation. Thus a permanent increase in dosage rate results eventually in a permanently greater social burden. A temporary increase in radiation produces a temporary increase in social burden. But the effects of mutation will appear over many future generations, and the social burden will only slowly return to its previous equilibrium.

Some human mutations are dominant; they appear in heterozygotes, and so affect immediate offspring of irradiated persons. Many other mutations are nearly completely recessive: they appear only in homozygotes. They do not affect the immediate offspring of an irradiated person, but they will appear in subsequent generations when two heterozygotes marry.

What quantitative estimates can we make of the social burden due to radiation? The average generation time in man is 30 years, and the present annual dose of radiation per capita is 0.2 roentgen. The gonad dose, delivered to the male reproductive organs, is about half of this. Thus the gonad dose per generation is about 3 roentgens. It produces mutations at about 10 per cent of the spontaneous rate.

Only half of the present radiation dose has been with us long enough to produce a social burden in equilibrium. This is, of course, the radiation from natural sources.

Man-made radiation has only recently begun to take effect. Thus the present social burden from radiation is only 5 per cent of the total; it will eventually rise to 10 per cent if artificial sources continue at their present rates.

We can translate the same estimates into numbers of people. The present total genetic burden in the American population is about 3 per cent, or 6 million people. About 300,000 owe their disability to natural radiation, and a negligible number to artificial radiation. But if present man-made dose rates continue, future populations will contain an additional 300,000 people with inherited disabilities. This is a shocking number, even large enough to suggest that diagnostic and therapeutic radiation may ultimately cause more disease than it cures.

What would be the genetic result of fallout from weapons testing if it were continued at the past rate? From the hereditary standpoint it is fortunate that most fallout radiation is concentrated in the bones, so that the gonad dose is small. The estimated equilibrium rate is about 0.1 roentgen per generation, only 3 per cent of the rate from natural radiation. This still means that we could expect an eventual social burden of 10,000 people in the American population, if testing were to continue.

It is possible for heterozygous carriers of deleterious genes to be genetically more fit than homozygotes. When this is true, the population equilibrium is essentially independent of mutation rates; the social burden is controlled by the rates of survival of the two types of individuals. Some human genes behave this way, but probably not many. It is significant, however, that such genes contribute a disproportionate amount to the total social burden. Even if they are rare, they may represent an important fraction of our genetically sick.

We have discussed the degree to which a given genetic disorder creates a social burden. This need not be the same as the degree of genetic debilitation, which is measured only by the failure to produce offspring. To make the distinction clear, let us consider diabetes mellitus. Before the discovery of insulin therapy, diabetics left fewer offspring. Thus new mutations causing diabetes were counterbalanced by genetic debilitation. Now, however, insulin permits diabetics to be as genetically fit as normal people. New mutations are not being forestalled; the frequency of diabetes in the population is rising to a new equilibrium. But diabetes still produces a social burden. Diabetics are sick people who must undergo constant medication. Some proportion of our resources must be devoted to producing insulin, hypodermic needles, and other special accommodations for them.

Each time, therefore, that we relieve the genetic disability of an inherited disorder, we do not necessarily relieve the social burden of human suffering and labor. Moreover, since we are preserving the gene, we increase the fraction of affected people and the total social burden. It is good to bear such things in mind when we discuss the genetic effects of increasing the mutation rate by radiation. We must not lose sight of the fact that the social burden can increase enormously when we devote ourselves to saving the lives of people with genetic disorders.

This is, of course, the price we pay for our humanity. It is a price we shall continue to pay for as long as we remain essentially human. We have left the jungle, where the sick are abandoned to suffering and death. But we must keep ourselves aware of the rising cost of our essential humanity.