This interpretation of the course of events is more in keeping with the observations made during the field tests of gamma globulin and formalinized vaccine than is the hypothesis that the central nervous system is invaded directly across the blood vessels.

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Genetic Effects of Atomic Radiation

The coming of the atomic age has brought both hopes and fears. The hopes center largely around two aspects: the future availability of vast resources of energy, and the benefits to be gained in biology, medicine, agriculture, and other fields through application of the experimental techniques of atomic physics (isotopes, beams of high-energy particles, and so forth).

Gains in both of these areas can be of great benefit to mankind. Advances in medicine and agriculture are obviously desirable. The wide availability of power can also be of great benefit, if we use this power wisely. For not only should there be enough power to meet the more obvious and mechanical demands, there should be enough to affect society in much more far-reaching and advantageous ways, so as to reduce world tensions by raising the economic standards of areas with more limited resources.

On the other hand, the atomic age also brings fears. The major fear is that of an unspeakably devastating atomic war. Along with this is another fear, minor as compared with total destruction, but nevertheless with grave implications. When atomic bombs are tested, radioactive material is formed and released into the atmosphere, to be carried by the winds and eventually to settle down at distances which may be very great. Since it does finally settle down it has been aptly named "fallout."

There has been much concern, and a good deal of rather loose public debate, about this fallout and its possible dangers.

Are we harming ourselves; and are there genetic effects which will harm our children, and their descendants, through this radioactive dust that has been settling down on all of us? Are things going to be still worse when presently we have a lot of atomic power plants, more laboratories experimenting with atomic fission and fusion, and perhaps more and bigger weapons testing? Are there similar risks, due to other sources of radiation, but brought to our attention by these atomic risks?

What Complications Are Met in Reaching a Decision?

Now it is a plain fact, which will be explained in some detail later in this report, that radiations [Throughout this report, the word *radiation* is not used in its broadest sense, but refers primarily to gamma rays and/or x-rays and sometimes to other sorts of radiations.] penetrating the bodies of human beings are genetically undesirable. Even very small amounts of radiation unquestionably have the power to injure the hereditary materials. Ought we take steps at once to reduce, or at least to limit, the amount of radiation which people receive?

There are two major difficulties that make it very hard to decide what is

This article is the major portion of the text of the summary report of the Committee on Genetic Effects of Atomic Radiation. It is one of six reports prepared for the Study of the Biological Effects of Atomic Radiation by the National Academy of Sciences. The other five summary reports will be published in subsequent issues of *Science*. The members of the committee are Warren Weaver, Rockefeller Foundation, *chairman*; George W. Beadle, California Institute of Technology; James F. Crow, University of Wisconsin; M. Demerec, Carnegie Institution of Washington; G. Failla, Columbia University; H. Bentley Glass, Johns Hopkins University; Alexander Hollaender, Oak Ridge National Laboratory; Berwind P. Kaufmann, Carnegie Institution of Washington; C. C. Little, Roscoe B. Jackson Memorial Laboratory; H. J. Muller, Indiana University; James V. Neel, University of Michigan; W. L. Russell, Oak Ridge National Laboratory; T. M. Sonneborn, Indiana University; A. H. Sturtevant, California Institute of Technology; Shields Warren, New England Deaconess Hospital; and Sewall Wright, University of Wisconsin. The following changes have been made in the text: The "Foreword," the section entitled "Radioactive material and radiations," and the section entitled "Some basic facts about genetics" have been omitted. References to these sections in the remainder of the text have also been omitted (omissions are marked by ellipsis). A few additions, including a definition of radiation taken from one of the omitted sections and references from one section to another by title instead of number, have been made (additions are marked by square brackets). In addition, all units of measurement have been spelled out. The full texts of the summary reports are available from the National Academy of Sciences, and the texts of the technical reports will be published in monograph form by the NAS.

sensible to do. First, although the science of genetics is as precise and as advanced as any part of biology, it has in general, and particularly in human genetics, not yet advanced far enough so that it is possible to give at this time precise and definite answers to the questions: just *how* undesirable, *how* dangerous are the various levels of radiation; just *what* unfortunate results would occur?

Second, even if the relevant questions concerning radiation genetics could be answered definitely, that would be only part of the story. The over-all judgment (how much radiation should we have?) involves a weighing of values and a balance of opposing aims in regard to some of which the techniques of physical and biological science offer little help.

What is involved is not an elimination of all risks, for that is impossible—it is a balance of opposed risks and of different sorts of benefits. And the disturbing and confusing thing is that mankind has to seek to balance the scale, *when the risk on neither side is completely visible.* The scientists cannot say with exact precision just what biological risks are involved in various levels and sorts of radiation exposure (these considerations being on one pan of the risk scale); nor can anyone precisely evaluate the over-all considerations of national economic strength, of defense, and of international relations (all on the other pan of the scale).

Must We Move Entirely in the Dark?

Does this mean that geneticists have, at the moment, nothing useful to say on this grave subject? Fortunately, this is not the case. We do know something, though not nearly enough to give definite answers to a great many important questions. There is a considerable margin of uncertainty about much of this, and as a result, there are naturally some differences of opinion among geneticists themselves as to exact numerical values, *although no disagreement as to fundamental conclusions.* . . .

In relatively simple fields, where both theory and experiment have progressed far, a comforting kind of precision does often obtain. But it is characteristic of the present state of human radiation genetics that one must carefully and painstakingly note a lot of qualifications, of special and sometimes very technical conditions, of cautious reservations. The public should recognize that the attitudes and statements of geneticists about this problem of radiation damage have resulted from deep concern and from attempts to exercise due caution in a situation that is in essence complicated and is of such great social importance.

It is not surprising that our knowledge of genetics—and especially human radiation genetics—is so fragmentary. What goes on inside cells and the effects of radiations on these processes are extremely complicated and subtle problems. To attack them successfully requires a tremendous lot of time; for the inherent variability of certain of these effects is such that to establish something with certainty one must do not one experiment but many thousands of individual tests and observations. To attack these problems also requires a high degree of special skill—and perhaps most of all, imaginative ideas which can be tested.

Single-celled organisms, as well as fruit flies and corn plants, have been specially rewarding objects of genetic study. In evolutionary terms, however, insects and plants are clearly a long way from man, and we are really just beginning to get genetic information about the effects of radiation on some of the lower mammals, such as mice. Even so, several matters of profound importance have already become clear: bacteria or fruit fly, mouse or man, the chemical nature of the hereditary material is universally the same; the main pattern of hereditary transmission of traits is the same for all forms of life reproducing sexually; and the nature of the effects of high-energy radiations upon the genetic material is likewise universally the same in principle. Hence, when it comes to human genetics, where the impossibilities of ordinary scientific experimentation are clear and only a tantalizing start has been made, we can at least feel certain of the general nature of the effects, and need only to discover ways in which to measure them precisely.

How Could We Reduce Radiation Risk?

The major ways to reduce our present and future exposure to radiations would be: (i) to reduce medical and other use of x-rays as much as is feasible; (ii) to set and to observe regulations for the proper construction and safe operation of nuclear power plants and for the methods used to dispose of their radioactive wastes as well as the methods used in mining and processing the fissionable material; (iii) to reduce the testing of atomic weapons and hence to reduce radioactive fallout; (iv) to place limits on the human exposures involved in certain aspects of experimentation in atomic and nuclear physics.

To carry out the steps just mentioned would, in greater or lesser degree for the various items, reduce radiation risks. Progress with regard to step (i) can doubtless be achieved, although to go too far in reducing the medical use of x-rays would of course lead to the risk of poorer diagnosis and less effective treatment of disease. But to carry out steps (ii), (iii), and (iv) would subject us to a different set of risks. We might thereby impede progress in the nuclear field. We might seriously weaken our country's position in the world. We might deny future generations some of the possible benefits of nuclear power and of other atomic discoveries. . . .

Radiations and Genetic Mutations

. . . radiations, such as x-rays or gamma rays, can be . . . serious from the genetic point of view. For although the genes . . . normally remain unchanged as they multiply and are passed on from generation to generation, they do very rarely change, or *mutate*; and *radiation*, as we have already mentioned, *can give rise to such changes or mutations in the genes.* The change is presumably an alteration in the complicated chemical nature of the gene, and the energy furnished by the radiation is what produces the chemical change. Mutation ordinarily affects each gene independently; and once changed, an altered gene then persists from generation to generation in its new or mutant form.

Moreover, the mutant genes, in the vast majority of cases, and in all the species so far studied, lead to some kind of harmful effect. In extreme cases the harmful effect is death itself, or loss of the ability to produce offspring, or some other serious abnormality. What in a way is of even greater ultimate importance, since they affect so many more persons, are those cases that involve much smaller handicaps, which might tend to shorten life, reduce number of children, or be otherwise detrimental.

The changed character, due to the mutated gene, seldom appears fully expressed in the first generation of offspring of the person who received the radiation and thus had one of his genes mutated. For these mutant genes are usually recessive. If a child gets from one parent a mutant gene, but from the other parent a normal gene belonging to that pair, then the normal gene is very likely to be at least partially dominant, so that the normal characteristic will appear.

But . . . the harmful recessive mutant genes are not usually completely masked. Even when paired with a normal and dominant gene, that is to say even when in the heterozygous state, they still have some detrimental effect. This "heterozygous damage" is ordinarily much smaller than the full expression of the mutant when in the homozygous state, and yet there may be a significant shortening of the length of life or reduction of the fertility of the heterozygous carriers of the mutant. And the risk of heterozygous damage *applies to many more* *individuals*, indeed to every single descendant who receives the gene.

The relations of genes to ordinary traits (not to the most simply determined biochemical traits) are of course much more complex than the previous paragraph would seem to imply. Such gene-determined traits may vary from person to person, due perhaps to environmental differences, and often may not even appear at all. A single gene usually affects several such characters, and characters are practically always affected by many genes. Also the effect of a gene may depend on what other genes are present, often in a complex way. For example, a mutation tending to increase weight might be harmful to certain persons, but beneficial to others.

Indeed it is likely that a large fraction of the genes that determine normal variability are of this rather ambiguous type that are sometimes deleterious, sometimes not. Mutations within this sort would not necessarily be harmful. Such mutations presumably occur, but geneticists do not know what fraction of all mutations are of this type, for they are not ordinarily detectable. However, the mutations that form the basis of this report are those that are relatively detectable, and these, as mentioned earlier, are almost always harmful.

Individuals bearing harmful mutations are handicapped relative to the rest of the population in the following ways: they tend to have fewer children, or to die earlier. And hence such genes are eventually eliminated—soon if they do great harm, more slowly if only slightly harmful. A mildly deleterious gene may eventually do just as much total damage as a grossly and abruptly harmful one, since the milder mutant persists longer and has a chance to harm more people.

In assessing the harm done to a population by deleterious genes, it is clear that society would ordinarily consider the death of an early embryo to be of much less consequence than that of a child or young adult. Similarly, a mutation that decreases the life expectancy by a few months is clearly less to be feared than one that in addition causes its bearer severe pain, unhappiness, or illness throughout his life. Perhaps most obviously tangible are the instances, even though they be relatively uncommon, in which a child is born with some tragic handicap of genetic origin.

A discussion of genetic damage necessarily involves, on the one hand, certain tangible and imminent dangers, certain tragedies which might occur to our own children or grandchildren; and on the other hand certain more remote trouble that may be experienced by very large numbers of persons in the far distant future.

No two persons are likely to weigh exactly alike these two sorts of danger. How does one compare the present fact of a seriously handicapped child with the possibility that large number of persons may experience much more minor handicaps, a hundred or more generations from now?

There are thoughtful and sensitive persons who think that our present society should try to meet its more immediate problems and not worry too much about the long-range future. This viewpoint is in some instances supported by the belief that new ways, perhaps unimaginable at the moment, are likely eventually to be found for meeting problems.

There are other thoughtful and conscientious persons who think that we are specifically responsible for guarding, as well as we can now determine, the long future.

Recognizing the inevitability and propriety of both viewpoints, and recognizing that they lead different persons to express their concerns through different examples and with differing emphases, the fact of major importance for this present study is that, traveling by different routes, different geneticists arrive at the same conclusion: *Complexities notwithstanding, the genetic damage done, however felt and however measured, is roughly proportional to the total mutation rate.*

Mutant Genes and Evolution

Many will be puzzled about the statement that practically all known mutant genes are harmful. For mutations are a necessary part of the process of evolution. How can a good effect—evolution to higher forms of life—result from mutations practically all of which are harmful?

First of all, it is not mutations which, of themselves, produce evolution, but rather the action of natural selection on whatever combinations of genes occur. Much of the evolutionary progress probably depends on changes within the range of normal variability, and thus depends on genes of very small effect, and of the type mentioned in the previous section which are favorable or unfavorable depending on what other genes are present. Thus evolution consists of a complex shifting of frequencies of such genes, accompanied by the continuous process of elimination of detrimental mutations and the occasional incorporation into the population of a favorable mutation.

Nature had to be rather ruthless about this process. Many thousands of unfortunate mutations, with their resulting handicaps, were tolerated, just so long as an advantageous mutation could be utilized, once in a long while, for inching the race up slightly higher to a better adjustment to the existing conditions. The rare creature with an advantageous combination of genes was better fitted to survive and displace his less favored companions, and thus evolution was served, even though there were thousands of tragedies for every success.

The reader may be troubled by a second difficulty. If mutation results in at least some favorable types, and if these are building blocks of evolution, why is an increase in mutation rate regarded as undesirable? Why would not an increase in mutation rate produce a larger total number of the favorable types and so speed up evolution? If the favorable types are normally quite rare, would it not almost seem that increasing the mutation rate would be desirable? The answer to this question lies in the consideration that the bad effects of mutation must be balanced against the good. Some mutation is necessary for evolution, but if the mutation rate is too high, the unfavorable mutations will be so numerous that the species and its future evolution will be handicapped. Under present-day conditions of living and medical care, it seems unlikely that the unfavorable results of mutation are being eliminated nearly as rapidly as was formerly the case. In other words, one of the consequences of the amazing mastery of his environment which man has achieved has been an actual decrease in the severity of natural selection.

Geneticists in fact believe that although favorable mutations are rare compared with unfavorable ones, the human population probably already has, and will continue to have as a result of its present mutation rate and without additional mutations from increased radiation, a large enough total supply of favorable, partially favorable, and potentially favorable mutations. In other words, with our present mutation rate we shall continue to have a degree of genetic variability adequate for further evolution.

What Can Geneticists Say To Help Resolve Our Problem?

With the background furnished by the preceding discussion, we can now state rather concisely certain main points on which geneticists are in substantial agreement. Some of these points will partially repeat statements already made, but they are included here in order that this section be reasonably complete of itself.

1) Radiations cause mutations. Mutations affect those hereditary traits which a person passes on to his children and to subsequent generations.

2) Practically all radiation-induced mutations which have effects large enough to be detected are harmful. A

small but not negligible part of this harm would appear in the first generation of the offspring of the person who received the radiation. Most of the harm, however, would remain unnoticed, for a shorter or longer time, in the genetic constitution of the successive generations of offspring. But the harm would persist, and some of it would be expressed in each generation. On the average, a detrimental mutation, no matter how small its harmful effect, will in the long run tip the scales against some descendant who carries this mutation, causing his premature death or his failure to produce the normal number of offspring.

Although many mutations do disturb normal embryonic growth, it is not correct that all, or even that most mutations, commonly result in monstrosities or freaks. In fact, the commonest mutations are those with the smallest direct effect on any one generation—the slight detrimentals.

3) Any radiation dose, however small, can induce some mutations. There is no minimum amount of radiation dose, that is, which must be exceeded before any harmful mutations occur.

4) For every living thing—bacterium, fruit fly, corn plant, mouse, or man—there exists mutations which arise from natural causes (cosmic rays, naturally occurring radiations from radium and similar substances, and also from heat and certain chemicals). These naturally occurring, and hence unavoidable, mutations are usually called "spontaneous mutations."

Like radiation-induced mutations, nearly all spontaneous mutations with detectable effects are harmful. Hence these mutations tend to eliminate themselves from the population through the handicaps or the tragedies which occur because the persons bearing these mutants are not ideally fitted to survive.

We all carry a supply of the spontaneous mutant genes. The size of this supply represents a balance between the tendency of mutant genes to eliminate themselves, and the tendency of new mutants to be constantly produced through natural causes.

5) Additional radiation (that is, radiaation over and above the irreducible minimum due to natural causes) produces additional mutations (over and above the spontaneous mutations). The probable number of additional induced mutations occurring in an individual over a period of time is by and large proportional to the total dose of extra radiation received, over that period, by the reproductive organs where the germ cells are formed and stored. To the best of our present knowledge, if we increase the radiation by x percent, the gene mutations caused by radiation will also be increased by x percent.

The *total dose* of radiation is what counts, this statement being based on the fact that the genetic damage done by radiation is *cumulative*.

A larger amount of radiation produces a larger number of mutations. But within the limits of the radiation doses being considered in this report there is every reason to expect that these additional mutants would be of the same general sort as those produced by the natural background radiation. That is to say, mildly larger doses of radiation would produce *more*, but not *worse*, mutants.

6) From the above five statements a very important conclusion results. It has sometimes been thought that there may be a *rate* (say, so much per week) at which a person can receive radiation with reasonable safety as regards certain types of direct damage to his own person. But the concept of a *safe rate* of radiation simply does not make sense if one is concerned with genetic damage to future generations. What counts, from the point of view of genetic damage, is not the rate; it is the *total accumulated dose to the reproductive cells of the individual from the beginning of his life up to the time the child is conceived.*

What is genetically important to a child is the total radiation dose that child's parents have received from their conception to the conception of the child. Since this report necessarily deals with averages, the significant total dose period should be, at least approximately, the number of years that normally elapses from the conception of a person to the average time at which offspring are conceived. In the United States, based on 1950 data, the average age of fathers at the births of all children is 30.5 years, whereas the average age of both parents is 28.0 years. It therefore seems sensible for us to use the round figure of 30 years, especially since this figure is the one usually chosen to measure a generation. Using this 30-year figure for characterizing the "total reproductive life radiation dose" would have the result that about half of the total offspring would receive the possible effects of a smaller, and about half the possible effects of a larger, radiation dose.

7) The problems of defining and estimating genetic damage are very difficult ones. There are at least three different aspects which must be considered. The first aspect places emphasis on the risk to the direct offspring and later descendants of those persons who, from occupational hazard or otherwise, receive a radiation dose substantially greater than the average received by the population as a whole.

The second aspect refers to the effect of the *average* dose on the population as a whole.

The third aspect refers in still broader terms to the possibility that increased and prolonged radiation might so raise the death rate and so lower the birth rate that the population, considered as a whole, would decline and eventually perish. We are at present extremely uncertain as to the level of this fatal threshold for a human population. This is one reason why we must be cautious about increasing the total amount of radiation to which the entire population is exposed.

These three approaches to the problem of genetic damage involve estimating the damage in successive generations and also the total damage in all generations, due to an increase in the amount of mutation. The relative emphasis one places on these three aspects depends in part on whether one thinks primarily in terms of distress to individual persons, or whether one thinks in terms of the population as a whole. Necessarily involved is the contrast between manifest harm to a few, and less evident but no less unreal harm to many. Also involved is the contrast between a more short-term and a more long-range point of view.

One way of thinking about this problem of genetic damage is to assume that all kinds of mutations on the average produce equivalent damage, whether as a drastic effect on one individual who leaves no descendants because of this damage, or a wider effect on many. Under this view, the total damage is measured by the number of mutations induced by a given increase in radiation, this number to be multiplied in one's mind by the average damage from a typical mutation.

Measuring total damage in terms of the number of mutations does indeed necessarily involve this concept of the average damage from a typical mutation, and some geneticists find this concept difficult and illusive. They would point out that mutations may be grouped in classes that differ, on a subjective scale, many thousandfold in the amount of damage per mutation. As examples they would cite a mutation which results in very early death of an embryo (which might cause very little social or personal distress), and a mutation which results in severe malformation to a surviving child (which would cause very great personal distress and which clearly involves a social burden).

Rather than utilizing this concept of the average total damage per mutation, some geneticists prefer to start with a consideration of the tangible damage which occurs now, as a result of the current rate of mutation, and get an index of damage by multiplying this by the ratio of the expected new mutation rate to the current one. This procedure, however, admittedly deals with only *part* of the total damage; so an alternative difficulty faces those who prefer this procedure, namely the difficulty of estimating what part of the total damage they have dealt with.

As an illustration of the first aspect, suppose that 10,000 individuals were exposed to a large dose of radiation, of the order of 200 roentgens. Then perhaps 100 of the children of these exposed individuals would be substantially handicapped, this being in addition to the number handicapped from other causes. In this case the connection with the radiation exposure could be established by a statistical study.

As an illustration of the second aspect, suppose the whole population of the United States received a small dose of extra radiation, say 1 roentgen. Then there is good reason to think that, among 100 million children born to these exposed parents, there would be several thousand who would be definitely handicapped because of the mutant genes due to the radiation. But these several thousand handicapped children might be, so to speak, lost in the crowd. Society might be more impressed by the 100 more obvious cases of the preceding paragraph than by the more hidden several thousand cases of this paragraph.

We should not disregard a danger simply because we cannot measure it accurately or underestimate it simply because it has aspects which appeal in differing degrees to different persons. Two conclusions seem to be clear and of importance: We should proceed with due caution as regards all agents which cause mutations; and we should vigorously pursue the researches which will in time give us a more precise way of judging all aspects of the risk.

Approximate Estimates

Up to this point of the discussion, the conclusions of the geneticist are pretty clear; the mutant genes induced by radiation are generally harmful, and the harm cannot be escaped.

But as yet this report has not furnished much of a basis for converting these conclusions into practical advice. Remembering that we must eventually balance risk against risk, it is obviously desirable to try to learn, as definitely as circumstances permit, the answer to the question: *How* great would be the genetic harm done by various doses of radiation?

[A later] section ["How harmful are radiation-induced mutations?"] of this report will respond to this question. But before giving the various replies, there should be some preliminary explanation concerning the nature of the answers given.

Science, and particularly the branch which deals with the physical world about us, has succeeded in giving highly precise answers to many questions. When one talks about the velocity of light he does not need to say that it is *something like* 300,000 kilometers per second; he is justified in saying that it *is* 299,793 kilometers per second, and that the final integer is almost certainly not off by more than two units.

But when you ask an experienced surgeon what your chances are of surviving a serious operation, and if he answers "something like nine chances out of ten," then you accept that as a reasonable and helpful estimate. You do not distrust him because he gives you a rough estimate. Indeed you would have good cause to distrust him if he tried to give a highly precise answer.

In other words, there are many situations in which science can give only rough estimates. These estimates can nevertheless be very useful. No one should disdain such an estimate because it is rough, nor should anyone consider such estimates unscientific.

In [the] section ["How harmful are radiation-induced mutations?"] there will be stated the results of certain approximate calculations. The theory behind these calculations is on the whole well understood; but it is seldom the case that one knows with much accuracy the numerical values that enter into the calculations. One may, for example, say, "I don't know, in any direct measured sense, how many mutants would result if all the genes in a human fertilized cell received 1 roentgen of radiation. But using a pretty definitely known value for the mutation rate in certain genes of the mouse; and also knowing fairly well (in this case from experiments with fruit flies) how to pass from the measured rate for a few genes to the rate which probably applies to a germ cell as a whole; and then making the unfortunate but necessary assumption that these mouse and fruit fly figures apply reasonably well to man—using this procedure I come out with estimates for the number of mutants which would be produced in man by a given dose of radiation. Because of the uncertainties, I think it prudent to state not a single final result, but rather a range of result with estimated lower and upper limits. I wish that we had direct experimental evidence which would firm up this estimate. But I don't have to be too apologetic, for a large amount of biological reasoning has been successfully based on this sort of procedure. Man differs widely from lower forms of life in all the obvious, and in many other, respects. But the fundamental processes inside cells tend to be curiously alike, from the simplest creature of a single cell, up to man."

It may turn out that the uncertainties in quantities which enter the calculation are so great that the resulting uncertainty in the final answer is itself so very broad that the calculation simply does not furnish a useful estimate. But it may also turn out that, despite some considerable uncertainty in the constituent factors, the answer can be stated with a range of uncertainty which is small enough so that the estimate is useful.

It seems necessary to emphasize this matter of approximate estimation, so that no one will improperly conclude that a statement is unreliable because it involves a range of values. On the contrary, such a statement, when made in a situation like the present one, should be viewed as all the more dependable precisely because it does not pretend to an unwarranted accuracy.

How Much Radiation Are We Now Receiving?

If we are to talk about how harmful certain radiation doses may be, we should gain some idea of the amount of radiation we are already receiving from various sources.

The committee will release a report specially devoted to this particular subject, which summarizes in detail all the kinds, sources, and amounts of radiation. In the present report, only that minimum amount of information will be given which is necessary for our current discussion.

Neglecting several minor contributions (all of which will be treated in the longer report), man is at present receiving radiations from the following:

1) *Background radiation.* This is the radiation which results from natural causes (cosmic rays, naturally occurring radium, etc.) not under our control. Each person receives on the average a total accumulated dose of about 4.3 roentgens over a 30-year period. At high altitudes this dose is greater, because of the increase of cosmic rays. Thus this background is as high as 5.5 roentgens in some places in the United States.

2) *Medical x-rays.* According to present estimates, each person in the United States receives, on the average, a total accumulated dose to the gonads which is about 3 roentgens of x-radiation during a 30-year period. Of course, some persons get none at all; others may get a good deal more.

3) *Fallout from weapons testing.* The Atomic Energy Commission (under the Department of Defense, other measurements relating to fallout are also being made) is doing a technically competent and a socially conscientious job of measuring fallout, but it does not follow from this that one can answer, with high precision, all questions about the biological risks involved. What they usually measure (which, technically speaking, is a

beta-ray activity in air) has to be translated over into what is genetically important (namely, the gamma ray dose to the gonads). The estimation of the latter of these quantities from the former is a pretty complicated business.

Beside those just mentioned, there are certain further uncertainties in the fallout values. The measurements are necessarily taken far apart, and there is known to be considerable local variation due to meteorological conditions and topography. The radioactive dust, when it settles out of the air, is subject to weathering, as when it is washed off buildings by the rain and carried to locations where it may affect fewer persons. Also individuals inside houses, or other shelters, will be considerably less exposed than those in the open air.

Thus one cannot expect figures on fallout to be very precise ones. We have been informed that the AEC scientists are confident that the actual true dose figures are less than 5 times their stated estimates, and are also greater than one-fifth of these stated estimates.

It should be noted that the figures on fallout as stated by the Atomic Energy Commission make only a conservative correction for weathering and shelter; and thus their figures, at least in regard to this point, tend to overstate the danger rather than the opposite.

With these understandings, it may be stated that United States residents have, on the average, been receiving from fallout over the past 5 years a dose which, if weapons testing were continued at the same rate, is estimated to produce a total 30-year dose of about *one-tenth of a roentgen*; and since the accuracy involved is probably not better than a factor of 5, one could better say that the 30-year dose from weapons testing if maintained at the past level would probably be larger than 0.02 roentgen and smaller than 0.50 roentgen.

The rate of fallout over the past 5 years has not been uniform. If weapons testing were, in the future, continued at the largest rate which has so far occurred (in 1953 and 1955), then the 30-year fallout dose would be about twice that stated above. The dose from fallout is roughly proportional to the number of equal-sized weapons exploded in air, so that a doubling of the test rate might be expected to double the fallout.

The figures just stated are based on all information now available from both the Atomic Energy Commission and the Armed Forces and have been estimated as part of a study carried out for this committee by John S. Laughlin, chief of the Division of Physics and Biophysics, Sloan-Kettering Institute, and Ira Pullman, loaned to this study by the Nuclear Development Corporation of America. In their estimation correction has been made for weathering and shelter effects in accordance with the latest experimental data.

4) *Atomic power plants.* As yet the general population has not received radiation from atomic power plants or from the disposal of radioactive wastes. These are future sources of radiation that might become dangerous.

5) *Occupational hazards.* The preceding four points apply to everyone. Unless proper precautions are taken, persons who are close to equipment emitting x-rays, who are engaged in experimental work in atomic energy, who operate atomic plants, who test weapons, who mine or otherwise handle radioactive material, and so forth, are subject to the risk of greater radiation exposure during their work.

How Harmful Are Radiation-Induced Mutations?

As has already been indicated, there are various ways of estimating genetic harm, various attitudes which can be taken as to what is most serious and significant. But this situation should not be allowed to confuse or conceal the massive fact that, by whatever chain of argument or reasoning, all geneticists come out with the same basic conclusions.

1) Thus the first and unanimous reply to the question posed by the title to this section is simply this: *Any radiation is genetically undesirable,* since any radiation induces harmful mutations. Further, all presently available scientific information leads to the conclusion that *the genetic harm is proportional to the total dose* (that is, the toal accumulated dose to the reproductive cells from the conception of the parents to the conception of the child). This tells us that a radiation dose of $2X$ must be presumed to be twice as harmful as a radiation dose of X; but it still does not tell us the amount of harm we would be doubling.

2) Second, we remember that mankind has for ages been experiencing, as the so-called "spontaneous mutations," a certain rate of (generally harmful) mutations due to natural and uncontrolled causes (cosmic rays, heat, chemicals, and so forth). It is not entirely unnatural to think of this burden of mutations as a sort of "normal" burden on society (there is some basis for hoping that we may eventually be able to control at least a part of both spontaneous and radiation-induced mutations). Therefore it seems to be illuminating to ask: How much additional "man-made" radiation will it take before this "natural" amount of genetic mutation (to which we are at least in some senses adjusted) will be doubled?

The calculations which lead to an estimate of this "doubling dose" necessarily involve the rates of both spontaneous and radiation-induced mutations in man. Neither of these rates has been directly measured; and the best one can do is to use the excellent information on such lower forms as fruit flies, the emerging information for mice, the few sparse data we have for man—and then use the kind of biological judgment which has, after all, been so generally successful in interrelating the properties of forms of life which superficially appear so unlike but which turn out to be so remarkably similar in their basic aspects.

In view of the inevitable uncertainties, it is rather surprising that the final estimates, as made by numerous specialists of this committee and in other countries, do not differ more than they do. The lowest figure which has been responsibly brought forward for the doubling dose is 5 roentgens, and the largest estimates range up to 150 roentgens or even higher. Recent work with mice (which are, after all, mammals) gives some basis for thinking that the doubling dose is not as high as 150 roentgens. The experience in Japan gives some basis for thinking that the doubling dose is larger than 5 roentgens. Indeed it is clear that the doubling dose must be at least as large as the background radiation (which is between 4 and 5 roentgens, over 30 years, in the United States). This, in fact, would be the value of the doubling dose if spontaneous mutations were due to background radiation alone, heat and chemical agents making no contribution.

Thus various arguments reduce the 5–150-roentgen range, and several experienced genticists have recently made estimates in the narrower range of 30 to 80 roentgens.

In summary, then, of this particular point: Each individual, on the average, inevitably experiences during his reproductive lifetime a certain number of harmful spontaneous mutations from natural causes. He would experience an additional *equal number* of harmful mutations if he received a certain dose of radiation during that same period. This is known as the "doubling dose." The actual value of the doubling dose is almost surely more than 5 roentgens and less than 150 roentgens. It may very well be from 30 to 80 roentgens.

The first portion of this section said that twice as much radiation gives twice as much harm. This second portion goes a bit further. It says that something like 30 to 80 roentgens (or at a further extreme, 5 to 150 roentgens) of extra radiation dose would do mankind twice the harm it is now experiencing from spontaneous mutations.

3) The two preceding portions of this section are clearly not really satisfying. They do indicate in quantitative terms

how increases in radiation increase the harm. But anyone still wants to know in more specific terms, if possible, *how serious* is this harm that we may be doubling. If city traffic increases until the risk of crossing the street is doubled, then we will presumably still cross the street; for the risk per crossing is, after all, a very small one. If highway traffic increases until the risk in taking a 1000-mile drive is doubled, then many persons might well hesitate, for the risk is now unpleasantly high.

And this is the point at which it becomes most clearly evident that different geneticists find meaningful rather different approaches to the problem of genetic damage.

As has been stated previously, from one point of view the best index of genetic damage is the totality of tangible genetic defects of living individuals—say such things as mental defects, epilepsy, congenital malformations, neuromuscular defects, hematological and endocrine defects, defects in vision or hearing, cutaneous and skeletal defects, or defects in the gastrointestinal or genitourinary tracts. Roughly 4–5 percent of all live births in the United States have defects of this sort; and of all of these, perhaps about half—or 2 percent of the total live births—have simple genetic origin and appear prior to sexual maturity.

If mankind were subjected to a "doubling dose" of radiation, then the present level of 2 percent of such genetic defects would rise, and would eventually be doubled. More explicitly, consider the next 100 million births in the United States. This is about the number of children that will, in the future, be born to the presently alive population of the United States. Of these 100 million children, something like 2 million will experience genetic defects of the sort listed, these resulting from the deleterious "spontaneous" mutant genes which have been induced by natural causes excluding man-made radiation. If we were to be subjected, generation after generation, to an additional doubling dose of man-made radiation, then this present tragic figure of 2 million would gradually increase by 2 million more cases, up to an eventual new total of 4 million. It would, to be sure, take a very long time to reach this equilibrium double value. Perhaps 10 percent of the increase, or 200,000 new instances of tangible inherited defect, would occur in the first generation.

Since at various places this report considers a radiation dose of 10 roentgens, it may be useful to state the tangible inherited defects from a dose of that size. A dose of 10 roentgen would, on the above basis, give rise to some 50,000 new instances of tangible inherited defects in the first generation, and about 500,000 per generation ultimately, assuming of course an indefinite continuation of the 10-roentgen increased rate and also assuming a stationary population.

These figures by no means measure *all* the genetic damage that would result from a doubling dose; but they do make tangible and impressive the fact that a doubling dose of radiation would cause real personal and social distress.

4) There is another way of looking at this problem of genetic damage, and that consists of trying to make some useful sort of really long-term, fully complete estimate. This consists of estimating the total number of mutant genes which would be induced in the whole present population of the United States and passed on to the next appearing 100 million children, were this whole population to receive a certain total radiation dose to the gonads. In this instance we will use a dose of 10 roentgens, since a dose of that magnitude appears later in this report in the recommendations. Having estimated this total number of transmitted mutants induced by a dose of 10 roentgens, one then can only say, when he wishes to translate this over into harm or damage, that each one of these mutants must eventually be extinguished out of the population through tragedy. This statement does not, of course, hold in the detailed sense that one thinks of tracing each individual mutant gene until the line which bears and transmits it is overcome by the accumulating handicaps it imposes. The statement holds only in a statistical sense. Some lines of mutant genes will die out merely through normal chance procedures of inheritance. Others will multiply through these same chance procedures. But these normal chance effects cancel out; and the *statistical extinction* of the mutant genes is accomplished only through tragedy.

Concerning these estimates of total number of mutants, three things should be said. First, they are clearly not really satisfactory to any geneticist. Too much has to be assumed, too little is dependably known.

Second, this kind of estimate is not a meaningful one to certain geneticists. Their principal reservation is doubtless a feeling that, hard as it is to estimate numbers of mutants, it is much harder still, at the present state of knowledge, to translate this over into a recognizable statement of harm to individual persons. Also they recognize that there is a risk involved in extrapolating from mouse and *Drosophila* data to the human case.

Various remarks can, however, fairly be made in favor of this estimating attempt. Two largely independent methods lead to about the same results, and this increases one's confidence. Although the extreme ranges of the estimates differ widely, the mean estimate for any one geneticist is not very different from the mean for any other. Even the "guessing" which is involved hardly deserves that name, for it is based on long years of experience.

So that the final thing that should be said is that in spite of all the difficulties and complications and ranges in numerical estimates, the result is nevertheless very sobering.

Six of the geneticists of this committee considered the following problem: suppose the whole population of the United States received one dose of 10 roentgens of radiation to the gonads. What is the estimate of the total number of mutants which would be induced by this radiation dose and passed on to the next total generation of about 200 million children? Each geneticist calculated what he considered to be the most probable estimate, and then bracketed this by his minimum and maximum estimates. Each thus said, in effect: "I feel reasonably confident that the true value is greater than my minimum estimate and less than my maximum. My best judgment, as stated in a single figure, is what I have labeled the most probable estimate."

The most probable estimates as thus calculated by the six genticists do not differ widely. They bunch rather closely around the figure 5 million. Four of the six estimates are very close to that figure, and the other two differ only by a factor of 2.

These six geneticists concluded, moreover, that the uncertainty in their estimation of the most probable value was about a factor of 10. That is to say, their minimum estimates were about 1/10, and their maximum estimates about 10 times the most probable estimate.

This calculation assumes a stable value for the total population. This calculation is admittedly somewhat complicated and disappointingly vague. It is, to some geneticists, not a very meaningful way of looking at the problem. To others it adds up to something at least reasonably clear, and in any event very serious.

Fallout

There has been concern about the possible genetic harm due to the fallout of radioactive material which results from the testing of atomic weapons. Certain aspects of this problem will be discussed in the reports of the other committees of this study (fallout on grazing and cropland; fallout in the sea and possible concentration in marine organisms; the distribution of fallout material by the winds and in the upper atmosphere; possible pathological damage due to long-lived isotopes built into our bones; and so forth. The present comments relate only to the question of genetic damage.

From the point of view of this committee there are two summary remarks that should be made. First, since *any* additional radiation is genetically undesirable the fallout dose is genetically undesirable.

Second, the fallout dose to date (and its continuing value if it is assumed that the weapons testing program will not be substantially increased) is a small one as compared with the background radiation, or as compared with the average exposure in the United States to medical x-rays.

Recommendations

In light of the considerations which have been reviewed by this committee, and which have been, at least in major outline, summarized in this report, this committee has several recommendations.

These recommendations should all be interpreted in the light of the basic fact that *any* additional radiation is genetically undesirable. Therefore our society should hold additional radiation exposure as low as it possibly can. If certain figures (such as 10 roentgens) occur in a recommendation, it should most emphatically not be assumed that any exposure less than that figure is, so to speak, "all right," nor should it be for a moment assumed that disaster will suddenly descend if one of these figures is exceeded.

In any case in which a figure is stated, it is with the idea: stay just as far under this as you can; do not consider that this is an amount of radiation which is genetically harmless, for there is no such figure other than zero.

Opposing the fact that any further radiation is genetically bad is the practical fact that further radiation, from certain sources at least, is probably inevitable. The factors which argue for an increase in radiation are not genetic, and should obviously be appraised by a group much more representative than this committee. Thus our recommendations will have to be evaluated by others, who must decide what decisions society should or must make. As geneticists we say: *keep the dose as low as you can.* Thus we recommend:

1) That, in view of the fact that total accumulated dose is the genetically important figure, steps be taken to institute a national system of radiation exposure record-keeping, under which there would be maintained for every individual a complete history of his total record of exposure to x-rays, and to all other gamma radiation. This will impose minor burdens on all individuals of our society, but it will, as a compensation, be a real protection to them. We are conscious of the fact that this recommendation will not be simple to put into effect.

2) That the medical authorities of this country initiate a vigorous movement to reduce the radiation exposure from x-rays to the lowest limit consistent with medical necessity; and in particular that they take steps to assure that proper safeguards always be taken to minimize the radiation dose to the reproductive cells.

3) That for the present it be accepted as a uniform national standard that x-ray installations (medical and nonmedical), power installations, disposal of radioactive wastes, experimental installations, testing of weapons, and all other humanly controllable sources of radiations be so restricted that members of our general population shall not receive from such sources an average of more than 10 roentgens, in addition to background, of ionizing radiation as a total accumulated dose to the reproductive cells from conception to age 30.

4) The previous recommendation should be reconsidered periodically with the view to keeping the reproductive cell dose at the lowest practicable level. If it is feasible to reduce medical exposures, industrial exposures, or both, then the total should be reduced accordingly.

5) That individual persons not receive more than a total accumulated dose to the reproductive cells of 50 roentgens up to age 30 years (by which age, on the average, over half of the children will have been born), and not more than 50 roentgens additional up to age 40 (by which time about nine-tenths of their children will have been born.)

6) That every effort be made to assign to tasks involving higher radiation exposures individuals who, for age or other reasons, are unlikely thereafter to have additional offspring. Again it is recognized that such a procedure will introduce complications and difficulties, but this committee is convinced that society should begin to modify its procedures to meet inevitable new conditions.

Concluding Comments

The basic fact is—and no competent persons doubt this—that radiations produce mutations and that mutations are in general harmful. It is difficult, at the present state of knowledge of genetics, to estimate just how much of what kind of harm will appear in each future generation after mutant genes are induced by radiations. Different geneticists prefer differing ways of describing this situation: But they all come out with the unanimous conclusion that the potential danger is great.

This report recommends that the general public of the United States be protected, by whatever controls may prove necessary, from receiving a total reproductive lifetime dose (conception to age 30) of more than 10 roentgens of man-made radiation to the reproductive cells. Of this *reasonable* (not *harmless,* mind you, but *reasonable*) quota of 10 roentgens over and beyond the inevitable background of radiation from natural causes, we are now using on the average some 3 or 4 roentgens for medical x-rays. This is roughly the same as the unavoidable dose received from background radiation. It is really very surprising and disturbing to realize that this figure is so large, and clearly it is prudent to examine this situation carefully. It is folly to incur any x-ray exposure to the gonads which can be avoided without impairing medical service or progress.

The 10-roentgen recommendation applies in an average sense to the population as a whole. We also include a recommendation concerning the upper limit of exposure that any one individual should receive. These limits would of course apply to persons whose occupations involve radiation exposure, but they are intended as broad and uniform regulations which apply to any and every individual.

The fallout from weapons testing has, so far, led to considerably less irradiation of the population than have the medical uses—and has therefore been less detrimental. So long as the present level is not increased this will continue to be true; but there remains a proper concern to see to it that the fallout does not increase to more serious levels.

One important lesson which results from this study is the following: The present state of advance in atomic and nuclear physics on the one hand, and in genetics on the other hand, are seriously out of balance. We badly need to know much more about genetics—about all kinds and all levels of genetics, from the most fundamental research on various lowly forms of life to human radiation genetics. This requires serious contributions of time, of brains, and of money. Although brains and time are more important than money, the latter is also essential; and our society should take prompt steps to see to it that the support of research in genetics is substantially expanded and that it is stabilized.

We ought to keep all of our expenditures of radiation as low as possible. Of the upper limit of 10 roentgens suggested in recommendation 3, we are at present spending about one-third for medical x-rays. We are at present spending less—probably under 0.5 roentgen—for weapons testing. We may find it desirable or even almost obligatory that we spend a certain amount on atomic power plants. But we must watch and guard all our expenditures. From the point of view of genetics, they are all bad.