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

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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, radiation 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 com-

mittee 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.

OPINION

A Nuclear Paradigm Shift?

BUSINESS WORLD
By Holman W. Jenkins, Jr.

Wade Allison, emeritus professor of physics at Oxford, has a more realistic idea for fighting global warming than any being promoted at this week's climate summit in Paris: Increase by 1,000-fold the allowable limits for radiation exposure to the public and workers from nuclear power plants.

Politicians in Paris might notice their host country ranks 20th in per capita income but 50th in greenhouse emissions. You know why: France gets 75% of its electricity from nuclear. France has waded forward even while, for reasons having to do with horror of nuclear war and atmospheric testing, the world has surrendered since the 1950s to an unfounded dogma that radiation exposure is always dangerous in direct proportion to dose.

This is roughly the equivalent of saying a bullet fired at one foot per second has 1/900th the chance of killing you as a bullet fired at 900 f.p.s. (the actual muzzle velocity of a .45 automatic). Known as the linear no-threshold model (LNT), it underlies predictions of thousands of cancer deaths from Chernobyl or Fukushima that have consistently failed to be borne out.

Sweden a few years ago finally acknowledged nearly a year's supply of reindeer meat was needlessly destroyed after Chernobyl. A Japanese survey in 2013 found 1,600 premature deaths from "evacuation stress" (including suicides and loss of access to critical health care) among those forcibly protected from exposures that posed little or no threat and were less than residents of, say, Finland experience on a normal basis.

In 2001, America's then-chief nuclear regulator cautiously admitted that "excess cases of leukemia that can be attributed to Chernobyl have not been detected."

In the 1980s, 1,700 apartments in Taiwan were built from recycled steel contaminated with radioactive cobalt. In a 2006 study that found residents suffered unusually low cancer rates, the authors suggested that, by correcting our risk estimates, "many billions of dollars in nuclear reactor operation could be saved and expansion of nuclear electricity generation could be facilitated."

They were right: Exaggerated radiation fears have been crucial in driving up the safety, waste storage and licensing costs of nuclear power. But change may finally be coming—a paradigm shift in how we think about nuclear risk.

In June, the U.S. Nuclear Regulatory Commission began soliciting comments on whether to revise the safety standards in favor of a more sophisticated view, known as hormesis, which recognizes that organisms bathed in natural radiation have evolved cellular responses that protect against low-level radiation doses. The petitioners for this change include Dr. Carol S. Marcus, a professor of nuclear medicine at UCLA, who pointed to a lack of "scientifically valid support" for the LNT hypothesis and the "enormous" cost of "complying with LNT based regulations."

Kudos go to Mr. Allison and toxicologist Edward J. Calabrese of UMass Amherst, who've fought this battle for decades. Prof. Calabrese's latest paper, published in October in the journal Environmental Research, traces how a cabal of

U.S. regulators may radically revise safety assumptions about atomic radiation.

radiation geneticists associated with the Manhattan Project in the 1950s promoted adoption of the LNT hypothesis to increase the prestige of their discipline.

By now hundreds of papers have added evidence against LNT. A study last year from Munich's Institute of Radiation Biology showed a specific mechanism by which low levels of radiation induce a nonlinear response in certain cell protection mechanisms.

The consequences have been incalculable. Not from any intrinsic cost, safety or efficiency advantage coal became the world's go-to electricity source in the early 21st century. China and India today would not be opting for coal. They would be choosing among an array of off-the-shelf, affordable, safe and clean nuclear reactors developed in the advanced industrial countries.

How foolish have we been? In a month, coal mining kills more people than all nuclear power industry accidents since the beginning of time. Though it opens a can of worms, by the standards of LNT, coal is also more dangerous than nuclear. The particulates, heavy metals and radioactive elements coal plants emit are estimated to cause 13,200 deaths a year, according to the American Lung Association.

Put also into the mix Al Gore. When climate change politics emerged in the 1980s under his leadership, it quickly became a psychodrama in which ideological solidarity required rejection of nuclear power—though nuclear power is the obvious, easiest solution to the alleged carbon problem.

At least the Obama administration is capable of cold reason when not under the microscope from its lefty friends. Undoubtedly a prayer goes up daily from the White House that the greenies won't notice its openness to revising the nuclear safety standards. Maybe the Keystone pipeline distraction was good for something after all.

Unfortunately, it probably would take only one noisy New York Times op-ed accusing him of green apostasy to cause the president to surrender one of his few useful gestures on the climate conundrum.

Science

August 13, 2015

Carol S. Marcus, Ph. D., M. D.
Prof. of Radiation Oncology, of Radiological Sciences, and of Molecular and Medical Pharmacology (Nuclear Medicine)
David Geffen School of Medicine at UCLA
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Los Angeles, CA 900025-5014

Dear Dr. Marcus,

Thank you for your letter. Dr. McNutt has carefully reviewed the initial inquiry by Dr. Cuttler and has decided that *Science* will not be retracting the paper in question. Please find attached Dr. McNutt's response to Dr. Cuttler which includes a detailed explanation of the reasons behind this decision.

Best regards,

Anna Bashkirova
Executive Assistant to the Editor-in-Chief
SCIENCE Magazine

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From: Marcia McNutt <mmcnutt@aaas.org>
Date: Tuesday, August 11, 2015 at 6:07 PM
To: Jerry Cuttler <jerrycuttler@rogers.com>
Cc: "Doss, Mohan" <Mohan.Doss@fccc.edu>, Edward Calabrese <edwardc@schoolph.umass.edu>
Subject: Re: Science paper, Genetic Effects of Atomic Radiation; evidence of scientific misconduct

Dear Dr. Cuttler:

We considered carefully your concerns about the controversy with respect to the linear no-threshold (LNT) dose-response model for assessing the risk of radiation-induced cancer. You have requested that Science retract a 1956 paper that takes a position on this issue. Standard practice in Science and other journals would be not to consider the retraction of an article more than just a few years old except in extraordinary circumstances. New discoveries are constantly advancing the frontiers of science, and unless we had some statute of limitations on retractions, we would be constantly retracting old articles after the field has moved on. We can imagine certain exceptions in cases of papers that are still highly influential. In considering this specific request to Science, we asked the following questions:

(i) Is the 1956 Science paper trustworthy? We concluded that we cannot produce the information we need to answer this question 60 years post publication to the standards that would be required to consider a formal retraction. The authors are no longer living. We do not even have a record of the Science editorial standards of that era, much less a review jacket for that paper. This case is so old we would never be able to reconstruct the evidence from all parties involved in our editorial decision.

(ii) If the paper is not trustworthy, is the matter a problem of scientific quality or scientific integrity? Because we cannot answer (i), we cannot answer (ii). However, I will note that many of the concerns raised in the Calabrese paper would fall under the classification of science quality, not science integrity. They would not be grounds for retraction of a paper 60 years after the fact.

(iii) Does this Science paper still have the "pervasive influence" claimed in the article by Calabrese? We consulted an independent expert whose positions indicate that s/he has no extreme positions on this matter, one way or another. His/her considered view is that the 1956 Science paper was one of hundreds of papers over the past half century on this broad topic, and certainly the use of the LNT model by almost all the regulatory agencies, world wide, is now based on a lot more than the NRC report and Dr. Mueller's work. For example, if you take a look at the series of NRC "BEIR" reports, in the more recent ones there is no particular emphasis on Muller's work, with the arguments now more based on endpoints that more directly relate to radiation-induced cancer.

Based on this analysis, we do not see any reason to consider revising our policy for this paper. Science considers this case closed and will not reconsider the decision.

Sincerely,

Marcia McNutt

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August 11, 2015

Marcia K. McNutt, Ph.D.
Editor-in-Chief, *Science* Family of Journals
American Association for the Advancement of Science
1200 New York Avenue NW
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Subject: The article http://www.sciencemag.org/content/123/3209/1157 "Genetic effects of atomic radiation", a summary report of the Committee on the Genetic Effects of Atomic Radiation of the National Academy of Sciences, published in Science, in Volume 123, pages 1157-1164, on June 29, 1956,

Dear Dr. McNutt:

I would like to add my support to the request by Dr. Jerry Cuttler that ***Science*** retract the above summary report of the Genetics Panel of the Biological Effects of Atomic Radiation (BEAR) I Committee of the National Academy of Sciences (NAS). Prof. Edward Calabrese has summarized his findings regarding this report in a recent publication "On the origins of the linear-no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith" in Environ. Res. (2015), http://dx.doi.org/10.1016/j.envres.2015.07.011. There are many disturbing revelations regarding the origin of the LNT model in this comprehensive analysis by Prof. Calabrese. I will just mention one aspect in this letter.

The summary report made statements such as: *"Even very small amounts of radiation unquestionably have the power to injure the hereditary materials" and "there is no such figure other than zero" (for amount of radiation that is genetically harmless).* **The LNT model essentially originated with this report.** The report was also published in the New York Times and received huge publicity initiating the fear of low-dose radiation.

However, a year later, the letters exchanged among the BEAR Genetics Panel committee members included statements such as: *"I, myself, have a hard time keeping a straight face when there is talk about genetic deaths and the tremendous dangers of irradiation", "Let us be honest with ourselves—we are both interested in genetics research, and for the sake of it, we are willing to stretch a point when necessary", and "Now, the business of genetic effects of atomic energy has produced a public scare, and a consequent interest in and recognition of importance of genetics. This is to the good, since it will make some people read up on genetics who would not have done so otherwise, and it may lead to the powers-that-be giving money for genetic research which they would not give otherwise."* (Please see page 440 of the Calabrese article).

These exchanges are highly informative, as they indicate the true reason for the adoption of the LNT model was not that the smallest amount of radiation is dangerous according to the NAS BEAR Genetics Panel committee members, but their own self-interest.

The use of the LNT model over the years has resulted in tremendous public harm because of actions taken by governments, professionals, political activists, and the public based on unfounded fears and concerns regarding low-dose radiation. Some examples of public harm are as follows:

- Casualties in Fukushima: Urgent evacuation of the Fukushima area and its prolongation following the 2011 nuclear power plant accidents caused more than 1000 deaths with no recognizable benefit. More than 100,000 people remain displaced, either by government mandate or by fear of low-level radiation exposure.
- Suppression of nuclear energy: The use of nuclear energy to produce electricity, though it has proven to be the safest in terms of number of fatalities per amount of energy produced, has been suppressed due to trumped up low-dose radiation-induced cancer concerns. This has resulted in real casualties from the use of other non-nuclear energy sources.
- Suppression of research on cancer, Alzheimer's disease, etc.: There is considerable evidence supporting the use of low-dose radiation to prevent cancers and other major diseases like Alzheimer's. The use of the LNT model unnecessarily inhibits testing such ideas.
- Missed diagnoses: Many patients are refusing to have CT scans and doctors are not prescribing them due to radiation dose concerns, resulting in missed diagnoses and potentially harming patient health. Also, CT scans are being performed with poorer image quality to reduce radiation dose, making it harder to diagnose diseases.
- High costs: Ratcheting up of regulations for the various uses of radiation (medical, industrial, nuclear energy, etc.) has resulted in tremendously increased costs but no benefit.

Hence, both from the perspective of scientific integrity as well as in the best interests of the society, it is important that the LNT model be rejected by the scientific community and not be used any longer. The retraction of the 1956 BEAR I Genetics Panel summary report by ***Science*** would help in achieving this goal by correcting a major error committed by the scientific community in the 1950s. I hope you would initiate the process of retraction of the 1956 BEAR I Genetics Panel summary report immediately. Thanks for your consideration.

Sincerely,

Mohan Doss

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August 9, 2015

Marcia K. McNutt, Ph.D.
Editor-in-Chief, *Science* Family of Journals
American Association for the Advancement of Science
1200 New York Avenue NW
Washington, DC 20005

Dear Dr. McNutt:

I join with Jerry Cutler in asking you to retract the article by the Committee on the Genetic Effects of Atomic Radiation of the National Academy of Sciences: Genetic effects of atomic radiation. Science (123)1157-1164, 29 June 1956. This article is patently scientific fraud, as ably demonstrated by the detective work of Edward Calabrese: On the origins of the linear-no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith. Environ. Res. (2015), http://dx.doi.org/10.1016/j.envres.2015.07.011. This Science article is the bedrock upon which the erroneous LNT is based, and it is necessary to destroy that bedrock and leave the theory dangling.

The LNT is the basis of all radiation regulation in the United States and in those countries which accept the standards of the International Commission on Radiation Protection (ICRP), which is based upon the LNT. Recently I have petitioned the US Nuclear Regulatory Commission to change the basis of its radiation safety regulations by abandoning the LNT. There are two similar petitions pending. The retraction of the 1956 article by the prestigious journal *Science* would be most helpful in demonstrating that the supposed support for the LNT was in fact never there in the first place.

The ramifications of accepting the LNT are huge. There are enormous costs involved in the overregulation of nuclear power, radioactive waste disposal, medical uses, and research uses, to name a few. Levels for forced evacuation of people in the event of accidental or purposeful unleashing of radioactive material are absurd. The LNT is the basis of radiation fear and hysteria. It is not just costly in monetary terms, but in personal terms. A mother who refuses to let her child have a CT scan in the Emergency Dept. after a motor vehicle accident could end up stopping the physician from diagnosing a ruptured spleen and end up with her child bleeding to death. It is essential that the LNT be removed as the basis of radiation regulation.

I hope that you will carefully consider this request. Thank you for your attention and consideration.

Sincerely,

Carol S. Marcus, Ph.D., M.D.

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On the origins of the linear no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith

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ABSTRACT

This paper is an historical assessment of how prominent radiation geneticists in the United States during the 1940s and 1950s successfully worked to build acceptance for the linear no-threshold (LNT) dose–response model in risk assessment, significantly impacting environmental, occupational and medical exposure standards and practices to the present time. Detailed documentation indicates that actions taken in support of this policy revolution were ideologically driven and deliberately and deceptively misleading; that scientific records were artfully misrepresented; and that people and organizations in positions of public trust failed to perform the duties expected of them. Key activities are described and the roles of specific individuals are documented. These actions culminated in a 1956 report by a Genetics Panel of the U.S. National Academy of Sciences (NAS) on Biological Effects of Atomic Radiation (BEAR). In this report the Genetics Panel recommended that a linear dose response model be adopted for the purpose of risk assessment, a recommendation that was rapidly and widely promulgated. The paper argues that current international cancer risk assessment policies are based on fraudulent actions of the U. S. NAS BEAR I Committee, Genetics Panel and on the uncritical, unquestioning and blind-faith acceptance by regulatory agencies and the scientific community.

1. Introduction

In the course of recent assessments of the historical and scientific foundations of dose responses models, it was learned that the linear dose response model was deliberately promoted to advance ideological agendas of some of the world's most prestigious radiation geneticists (Calabrese, 2008; Calabrese, 2013a, 2015a, 2015b). These individuals intentionally misled/deceived the scientific and world communities at the highest possible levels, including in a 1946 Nobel Prize Lecture (Calabrese, 2011a; Calabrese, 2012), in their scientific publications (Calabrese, 2011b; Calabrese, 2013b; Caspari and Stern, 1948; Muller, 1950a, 1954; Uphoff and Stern, 1949), in their role as members of the U.S. NAS (Calabrese, 2013a; Calabrese, 2015b, 2015a) and in publications of the NAS [BEAR Committee, Genetics Panel – (Anonymous, 1956a; National Academy of Sciences NAS)/National Research Council NRC, 1956). Collectively, these deceptive actions became highly significant when they facilitated an unchallenged and blind-faith adoption of the Linear Dose Response (LDR) model for cancer risk assessment of ionizing radiation and later of chemical carcinogens (Calabrese, 2011b, 2013b, 2009a). The adoption of the LDR model affected the magnitude of financial resources involved in regulatory actions, toxic tort decisions and medical practices; it also affected risk communication messages to the general public, educational practices, governmental research funding priorities, as well as decisions related to lifestyle and child rearing.

The impact of these deceptions has been substantial and, to this day, they significantly affect and dominate regulatory policies and risk assessment practices. Since these disturbing findings were published as a series of separate papers in diverse scientific journals, (e.g. mutation, radiation and toxicology journals) (Calabrese, 2015b, 2015a, 2011c, 2012, 2011b, 2013b, 2009a, 2014a, Calabrese, 014b), it has become necessary to develop an integrated and holistic version of this complex story. In addition, newly unearthed materials on key individuals have been discovered and incorporated herein to clarify previous historical frameworks. Finally, critical feedback recently received from reviewers, editors and others in the research community has proven invaluable in tempering the perspective and improving the content and context of this assessment.

This paper follows an historical timeline, starting with the professional/scientific relationship between Hermann Muller and Curt Stern and their subsequent collaborations on ionizing radiation during the Manhattan Project. The many, and, at times, bizarre ways in which Stern tried to prevent acceptance of the threshold model supportive findings of Ernst Caspari, a member of

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0013-9351/

the Manhattan Project team, in order to promote the LNT model, are detailed. Muller's Nobel Prize Lecture with emphasis on his assessment of the nature of the dose response in the low dose range, especially in light of the Caspari findings, is critiqued, leading to an assessment of how he and Stern acted to cover up Muller's Nobel Prize Lecture deceit via obfuscation of the Manhattan Project findings and the strikingly false subsequent statements of Muller in the scientific literature. The paper then assessed how the leadership of Muller and Stern profoundly affected beliefs on dose response within the genetics community during the 1950s, especially seen through the actions of the NAS BEAR I Genetics Panel in 1956 which assured the acceptance of the LNT by falsifying and fabricating the research record, thereby constituting scientific misconduct at the highest possible level.

2. The Curt Stern–Hermann J. Muller connections

Previously, this author had extensively researched the history of the non-linear (hormetic) dose–response model, its scientific foundations and its failure to thrive and out-compete the linear no-threshold (LNT) dose–response model during the first half of the 20th century (Calabrese, 2011b, 2005, 2009b; Calabrese and Baldwin, 2000a, 2000b, 2000c, 2000d, 2000e). As a continuation of this research activity, efforts have been exerted to assess in detail the historical and scientific origins that have resulted in the validation and acceptance of today's LNT model. During this investigation, it became evident that the role of Hermann J. Muller was essential to the adoption of the LNT model and needed greater clarification.

During this assessment of Muller, interest grew in the research activities of the Manhattan Project at the University of Rochester, especially those under the direction of Curt Stern who employed the fruit fly to investigate the nature of the dose response in the low dose range. Stern was of particular interest because he had a long personal and professional relationship with Muller that would markedly impact the LNT deception story. Stern had helped to organize the Fifth International Genetics Congress in Berlin during the fall of 1927 (Carlson, 1981). It was at this meeting that Muller first presented his landmark findings on X-ray-induced mutations in fruit flies (Muller, 1927, 1928), research that would eventually lead to his Nobel Prize in 1946 (Muller, 1946a). Later, Muller and Stern would have a conflict over Muller's deliberate failure to acknowledge a prior discovery by Stern that provided proof for the linear arrangement of genes, an issue that was then a very significant question in biology. Stern would challenge Muller on this point directly via a carefully documented letter dated August 8, 1929 [American Philosophical Society (APS) (American Philosophical Society, 1929a). Stern informed Muller that his earlier publication in Biologischen Zentrablatt (September, 1926) addressed the “theory of the linear arrangement and have specifically stated it in the title of the paper”. Stern concluded his letter to Muller with the statement that his manuscript "had been written before your [Muller's] first papers about them appeared." Nearly six weeks later, in a letter dated October 3, 1929, Muller would respond “I am very sorry to have omitted mention of your work in my discussion of translocation and not to have given you credit for having made the first cytological demonstration of a genetically demonstrated translocation and pointed out its significance for the theory of linear arrangement”. He then indicated that he had enclosed a “carbon copy of a note I am sending in on the subject to the American Naturalist, which I hope you will consider as rectifying this mistake” (American Philosophical Society, 1929b). While Stern caught Muller in a significant professional indiscretion, he let Muller “control” the narrative by not objecting to Muller's version of the correction. Nonetheless, this arrangement proved to be acceptable to Stern as seen in an October 23, 1929, letter from Stern to Muller, restoring a positive tone to their relationship (American Philosophical Society, 1929c). One could speculate what might have happened to the LNT story if Muller and Stern had not reconciled, possibly preventing Muller's involvement in the Manhattan Project as described below.

3. The Manhattan Project: Curt Stern and LNT

After Stern[1] initiated research on the Manhattan Project in 1943, he contacted Muller, then a professor of biology at Amherst College (1940–1945), to serve as a consultant to the project. Under normal circumstances this might have been routine, but Muller had a questionable past, abandoning the US to live and research in the Soviet Union from about 1934–1938 (Carlson, 1981). Stern nonetheless obtained approval by the U.S. government for Muller's participation in the radiation genetics project. Muller's involvement proved to be extensive, involving detailed technical written communications with Stern and other team members, visits to the University of Rochester, and a donation of his Muller-5 strain of Drosophila (Calabrese, 2011c).

The Manhattan Project of Stern was designed to expand the study of high dose ionizing radiation on genomic mutations to include the area of chronic, lifetime exposures at relatively low doses and very low dose rates. The first experiment under Stern's direction was an acute (i.e., short duration) exposure study over a broad dose range. It was conducted by Warren Spencer, a professor at the College of Wooster with a PhD from Ohio State University in the area of Drosophila biology. Previous research by several of Muller's students (Hanson and Heys, 1929, 1932; Oliver, 1930, 1931), at very high doses and over a limited dose range, provided support for the hypothesis that the nature of the dose response for X-ray-induced mutation was linear.

In the Spencer study, the effects of X-rays were assessed on sex-linked recessive lethality using Drosophila with acute/short term (2–40 min) exposures and a dose-rate ranging from 10 to 96 r/h. This resulted in a range of cumulative doses from 4000 r down to 25 r (i.e., lowest cumulative dose yet tested). Following a data collection period from December, 1944 to June, 1955, Spencer reported that X-rays induced gonadal mutations in a manner that were linear across the dose response continuum, just as Stern and Muller had predicted (Calabrese, 2011c).

Ernst Caspari, a Ph.D. in insect behavior, directed the next study. From October 1945, to August 1946, Caspari assessed the effects of gamma rays on Drosophila sex-linked recessive lethality. In Caspari's study the females were first mated, placed on an egg laying suppression diet, and then exposed to the gamma radiation (2.5 r/day) for 21 days with sperm stored in the female's spermatheca. In the Caspari study, there was an aging component to the sperm that was not in the Spencer study. The dose rate used in Caspari's study was much lower (13,200 times lower) than that used in Spencer's acute study at the same cumulative dose (Calabrese, 2011c).

The data from the chronic exposure study of Caspari supported a threshold dose–response model. Stern initially rejected the

[1] In the case of the University of Rochester mammalian radiation geneticist Donald Charles, despite the use of over 400,000 mice, his research was largely unproductive, with no methodologically-based technical publications during the time of the Manhattan Project which ended in 1946 (see Charles (1950) for a brief descriptive paper). An additional summary paper (Charles et al., 1961) was published [after Charles's death (Anonymous, 1955a) that tried to salvage the research effort with no obvious success. The failure of Charles to deliver a scientifically significant product for the Manhattan Project, given the level of resources directed to it, represented a substantial failing.

interpretation of Caspari as seen in written correspondence (American Philosophical Society, 1947a). Stern thought the findings were aberrant due to an unexpectedly high mutation rate of the "controls" that obscured a linear dose response, yielding only the appearance of a threshold response. Despite this rejection by his mentor, Caspari dug into the published literature and found convincing support for his rather than Stern's interpretation (Kaufmann, 1947; Muller, 1945, 1946b; Rajewsky and Timofeef-Ressovsky, 1939). To his credit, Stern accepted the data-based argument of Caspari.

Caspari's data were unexpected and somewhat troubling to him because they challenged the linear paradigm of the radiation genetics community. Therefore, Caspari decided to send his findings to another leading researcher, Milisav Demerec, head of genetics at Cold Spring Harbor, for review and comment. Caspari was looking for a way around this problem (i.e., alternative interpretation) and hoping that the influential Demerec might offer a solution. Reflecting the bias of the radiation genetics research community at this time, Demerec wrote back to Caspari, acknowledging the problematic nature of the data, and rather than himself providing the hoped for insight, asked Caspari what could be done to "save the hit theory" (American Philosophical Society, 1947b). There was little question that the Caspari data had created a problem and, in fact, it would be referred to by Stern as a "problem" in future correspondence [Letter of Stern to Noviski – (American Philosophical Society, 1948). Demerec would later become a member of the BEAR I Committee, Genetics Panel that recommended the acceptance of the linear dose–response model.

While Stern seemed to accept Caspari's findings that supported the validity of his control data, he nonetheless challenged the authenticity of the data in other ways. The manuscript that Stern and Caspari developed in the late summer/early fall of 1946 contained a six-page discussion, mostly arguing that Caspari's (rather than Spencer's) findings should not be accepted until it could be shown why his threshold-supporting data differed from the earlier linear dose–response findings of Spencer. This position, in and of itself, was problematic in that the two papers had several dozen important methodological differences (e.g., temperature of 18 °C vs. 24 °C, egg-laying suppression vs. enhancement diets, irradiation by X-rays vs. gamma rays, young vs aged sperm, male vs female exposures and numerous other differences – [see Table 2, (Calabrese, 2011c), making it virtually impossible (if not impractical) to resolve the differences.

Even though the Caspari study adopted technical and methodological improvements over the Spencer study and had avoided serious operational errors of the Spencer study (e.g., Spencer's failure to control temperature, his combining of treatment groups with the same cumulative exposure but with dose rates that differed by up to 2.5 fold, his failure to match control and treatment groups over the same time periods, and his inconsistent calibration of the X-ray machine, etc.) and errors in the modeling of low dose responses (see detailed criticisms – (Bonnier and Lüning, 1949; Bonnier et al., 1949), it was strangely the Spencer study with its linear dose response that became the gold standard and not the Caspari study.

Discussion in the Caspari paper, as noted above, made it clear that the findings in support of a threshold should not be accepted until the differences between the two papers could be resolved. As untenable as this position was, Stern's actions were even more inexplicable as he would not place a similar constraint upon the flawed Spencer paper that supported linearity. It is bizarre, if not unheard of, for investigators to ask the scientific community not to accept the validity of their findings until it could be reliably determined why their findings differed from a study of considerably lesser quality and reliability. Moreover, not placing at least the same constraints on the weaker study, for which Stern was also a co-author, calls into question the investigator's non-biased and objective approach to research. As a very accomplished scientist, Stern should have known that resolving differences between these two studies was not realistically possible.

Stern's unusual behavior makes sense when viewed as an attempt to blunt any challenge to the linear dose–response model (i.e., by demanding that the data of Caspari not be accepted). Stern ensured the success of this strategy by sending the Spencer and Caspari manuscripts to his own journal, *Genetics*, and by fully controlling their publication, including the Caspari discussion. There is no evidence that he submitted either of the papers for an independent peer review as the papers were submitted to the journal on November 25, 1947, and published less than five weeks later in January 1948 (Caspari and Stern, 1948; Spencer and Stern, 1948).

At this point it was not clear whether Muller had seen the Caspari data prior to his Nobel Prize Lecture on December 12, 1946. During the Lecture he disavowed any possibility that a threshold dose response could occur in the induction of mutations by ionizing radiation. He demanded a switch to the linear dose–response model, stating, "there is no escape from the conclusion that there is no threshold" (Muller, 1946a). Not knowing whether Muller had seen Caspari's data in support of a threshold model prior to his Nobel Prize Lecture, several science historians with considerable knowledge of Muller and that era were then contacted. Yet, none of these attempts answered the question. Fortunately, substantial correspondence between Muller and Stern, Caspari, Spencer and others was obtained from archival libraries. The archived records revealed that Stern wrote to Muller on September 24, 1946, to request his services in reviewing the Caspari manuscript in preparation for journal submission. A follow-up letter from Muller on September 27, 1946, accepted this invitation and on November 6, 1946, Stern sent the manuscript to Muller at the University of Indiana. On November 12, 1946, Muller acknowledged receipt of both the letter and the manuscript. He also indicated that he had briefly read the manuscript and recognized that the findings supported a threshold dose response, seriously challenging the linear model. Muller strongly encouraged Stern to find the means to undertake a replication study and indicated that he would try to provide a detailed evaluation prior to his Nobel Prize trip to Europe in early December. Clearly, this November 12th letter acknowledged that Muller had seen Caspari's data, understood the challenge to the linearity model, was not dismissive of the findings and acknowledged Caspari's competence and the need to repeat the findings (see Table 1 for the series of Stern/Muller correspondence statements).

Muller's evaluation of the Caspari manuscript occurred five weeks after his Nobel Prize Lecture in the form of a detailed letter to Stern dated January 14, 1947 (American Philosophical Society, 1947c). Based on this analysis, Muller had not changed his opinion. He unequivocally stated that he could not find any meaningful criticism of Caspari's work (i.e., "I have so little to suggest in regard to the manuscript.") and he restated the need to replicate the findings (i.e., "Unfortunately, therefore a replication seems to be imperative."). Thus, the statements written in private by Muller to Stern were those of a scientist, while his unequivocal public rejection of the threshold model at the Nobel Prize Lecture was deceptive and not without ideological underpinnings. Knowing that uncertainty existed in the low dose zone and that further study was needed, Muller could have acted more forthrightly by pronouncing his conditional rather than categorical support of the LNT model in Stockholm. Even four months later he remained steadfast and continued to advocate his unqualified support for the linear dose–response model. In a presentation to the New York Academy of Medicine in 1947, he stated that "there is then absolutely no threshold dose…and even the most minute dose carries a

Table 1
Letter correspondence demonstrating that Muller had seen and considered Caspari's threshold supportive findings prior to his Nobel Prize lecture on December 12, 1946 (American Philosophical Society, 1946/1947; Calabrese, 2011c).

September 24, 1946 – Stern to Muller:
"Dr. Caspari's report on his work is now being typed and I wonder whether we could bother you with sending you a copy for your new comments."

September 27, 1946 – Muller to Stern:
"Also, I'd be glad to see Caspari's paper too."

November 6, 1946 – Stern to Muller:
"Caspari's manuscript has finally been typed and we would appreciate very much your critical reading of it."

November 12, 1946 – Muller to Stern:
"I have just arrived from an absence of over 2 weeks and find the Caspari manuscript here waiting for me. Unfortunately, it catches me again when I am in a tremendous pressure of work, trying to make up both the trip just passed and for another one to come in a few weeks. However, I see that it is very important and shall do all I can to go through it in a reasonable time, surely before I leave again early in December. I hope that Caspari can wait that long if necessary. In the meantime I wonder whether you are having any steps taken to have the question tested again, with variations in technique. It is of such paramount importance, and the results seem so diametrically opposed to those which you and the others have obtained, that I should think funds would be fourth coming for a test of the matter. It is not, of course, that I doubt Caspari's reliability at all, but only that I naturally share the same doubts which he himself expressed. Of course, I am only judging by the summary and a quick glance through the paper, and have not had the opportunity to read the details."

definite chance of producing a change exactly proportional to the size of the dose" (Muller, 1948).

Muller's statement in a letter to Stern (American Philosophical Society, 1947c) about having "so little to suggest in regard to the [i.e., Caspari] manuscript" may not have been quite truthful, as Muller himself was most likely responsible for the only two changes introduced to the paper prior to its submission to the journal Genetics. With the exception of these two changes, the published study in Genetics was identical in every way to that paper which was sent to both Muller for his pre-submission review and to the Atomic Energy Commission (AEC) in 1947. In the journal version, the first and most significant change was the deletion of a key sentence in the Conclusion of the 1947 AEC version (Caspari and Stern, 1947). The deleted sentence is as follows: "From the practical viewpoint, the results presented open up the possibility that a tolerance dose for radiation may be found, as far as the production of mutation is concerned" (page 15). This statement indicated support for the threshold dose–response model. The second change was significant in that it added the name of Hermann J. Muller to the Acknowledgments of the published paper. It seems more than just coincidence that the only two changes imparted to the journal version consisted of (1) the deletion of a concluding statement in support of a threshold dose–response model and (2) the simultaneous addition of Muller's name to the acknowledgment section. There should be little doubt that removing the threshold conclusion statement was of profound benefit to Muller as it would help him sustain the ideological dominance of his favored LNT model. Muller clearly had the means, motive and opportunity to mitigate the threat imposed by Caspari's paper on the LNT model. So, was Muller responsible for deleting the key concluding sentence in support of a threshold model? Well, we may never know for sure, but strong circumstantial evidence seems to point in that direction.

In the aftermath of the Nobel Lecture, Stern followed Muller's suggestion to repeat the findings of Caspari. However, his two experienced doctoral researchers, Spencer and Caspari, had left for the College of Wooster and Wesleyan University in Middleton, Connecticut, respectively. Consequently, Stern tapped a new Master's student, Delta Uphoff, a recent graduate of Russell Sage College of Albany, New York, to replicate the Caspari research (Calabrese, 2011c). Data from her first experiment piqued Stern because her control values for mutation rates were about 40% below those found in the literature, including Caspari's study. Stern expressed his concern to Muller and also asked Muller to share his largely unpublished data with him on variation among controls for the mutation rates of aging sperm in the fruit fly. In a series of letters between Muller and Stern, Muller confirmed that the findings of Uphoff were not reliable and that the unpublished (and published) data were supportive of the Caspari control results. Muller's data led to an acknowledgment in the discussion section of the Uphoff and Stern manuscript (Uphoff and Stern, 1947) that the control group data were not interpretable and that the low control group value was most likely due to investigator bias. Thus, in a rather unprecedented move, Stern was quick to place blame on the inexperienced Uphoff. This manuscript, which importantly acknowledged the assistance of Muller, was sent to the Manhattan Project/AEC where it became classified and publicly unavailable. Thus, the acknowledgment by Stern of Uphoff's unreliable control data, together with the letter exchanges between Muller and Stern regarding the reliability of Caspari's control data, clearly indicated that Muller had strong confidence in the Caspari and not the Uphoff control data (Calabrese, 2011b).

Stern then had Uphoff undertake a follow up replication study. She again reported a similar unacceptably low control group response. As in the first case, the findings were again not interpretable. Finally, in a third experiment that was undertaken, another problem arose. This time it was not the control group, which seemed to respond as expected, but the treatment group whose response far exceeded that predicted by a linear dose–response model. At this point, Uphoff had finished her degree and eventually joined the National Institutes of Health (NIH) as a staff researcher. However, the damage was done to the Stern initiative regarding the Manhattan Project/AEC. Each attempt to replicate the Caspari findings had significant problems. Could anything be salvaged?

In January of 1949, Stern decided to submit a technical note to the journal *Science*, integrating the five major experiments conducted under his direction for the Manhattan Project/AEC. These involved the studies of Spencer and Caspari and the three Uphoff replications. In this *Science* paper, Stern attempted to rescue the first two Uphoff experiments that he already knew had aberrant control groups (Uphoff and Stern, 1947) and, according to multiple letter exchanges (Table 2), Muller also knew. Stern also chose to ignore certain data that were not in support of the linear model (Caspari and Stern, 1947) and, again attacked the Caspari study as aberrant even though nothing had changed except for the occurrence of even more data supporting the reliability of Caspari's

Table 2
Stern–Muller temporal letter exchange concerning the aged-stored sperm control mutation rate [see (Calabrese, 2015a) – supplement for a more complete letter exchange].

Curt Stern wrote a letter to Hermann J. Muller on January 22, 1947 (American Philosophical Society, 1947d) informing him that "At the present time it looks as if our new control data [probably the results of the first three months of the first Uphoff experiment; note that her first month's reading was an especially low mutation rate of 0.005%] for aged sperm are considerably below those of Caspari's." He then asked Muller to "send me your figures on rate of sex-linked lethal in sperm aged several weeks, (most desirably, if you have them, data on three weeks), in comparison to control data from non-aged sperm?"

On February 3, 1947 (Lilly Library, 1947) Muller answered by stating that "…. sperm of males which are about a week old and have been copulating freely [as in Caspari's experiment] during that period have only about 0.07 or 0.08 per cent of lethal. Thus the latter sperm, after three weeks, should contain something like 0.28 per cent of lethal."

control group. These multiple flip–flops by Stern were befuddling and surely required explanation, yet none were provided. The inferior Spencer study continued to receive strong support from both Stern and Muller even though, as noted above, it had very significant problems, none of which was noted by Muller in his letters to Stern regarding the research of Spencer, September 13, 1946 (American Philosophical Society, 1946) and Caspari on January 14, 1947 (American Philosophical Society, 1947c).

The *Science* paper of Uphoff and Stern (1949) was beneficial both to the LNT model and to Muller himself as its chief advocate. Stern was successful in artfully molding the interpretations of experimental data to fit the LNT mantra. He achieved this goal while the scientific community remained unaware that he and Uphoff (with Muller's support) had acknowledged just a year earlier that their own findings were not interpretable. Now, in the absence of any new data, these same findings were not only acceptable but also argued in support of the LNT model. And Caspari, who had successfully challenged Stern earlier, now remained silent as his findings in support of a threshold model were being undercut in favor of Muller's LNT model. As for Muller, he must have surely felt relief as he was spared the trouble of having to defend his highly deceptive comments at the Nobel Prize Lecture. Since the *Science* paper (Uphoff and Stern, 1949) was only a short one-page note, consisting mostly of a single table, Stern and Uphoff promised the science community a more detailed follow-up paper that would provide important methodological information and other relevant data. However, Stern and Uphoff never did publish the promised follow-up study and there exists no evidence that their colleagues in radiation genetics ever requested them to do so.

The strategy of Muller and Stern to deceive and obfuscate on the nature of the dose response in the low dose zone was successful. This is evidenced by the fact that the Spencer and Stern paper (Spencer and Stern, 1948) and the *Science* technical note by Uphoff and Stern became the highly influential and commonly cited papers. These "flawed" papers provided the scientific foundations upon which the linear dose response model was justified to the science community and, nearly a decade later, to the U.S. Congress at hearings (Congressional Hearings of 1957) partially inspired by the NAS report of the BEAR Genetics Panel (Calabrese, 2013a; Crow, 1957; Glass, 1957; Joint Committee on Atomic Energy, 1957; Muller, 1957). On the other hand, the technically superior and more relevant paper by Caspari in support of a threshold interpretation received virtually no attention; it was, in essence, unfairly but successfully marginalized. Various leaders in the field repeated false limitations of the Caspari study (Higgins, 1951; Jolly, 2004; Singleton, 1954) that were inspired by the deceptive comments of Stern and Muller e.g., (Muller, 1950b, 1954; Uphoff and Stern, 1949). For example Singleton (1954) echoed that Caspari's study could not be accepted because it had an aberrantly high control group. Ironically, this was Stern's original challenge that already had been so effectively rebutted by Caspari and Muller's own data (see Table 2 for letter exchange between Stern and Muller).

After the *Science* paper, Muller published several papers that repeatedly criticized Caspari's study as being too unreliable because of its high control group data. For example, in his 1950 article entitled "Some present problems in the genetic effects of radiation" in the *Journal of Cellular and Comparative Physiology,* Muller (1950a) provided an explicit characterization of the findings produced by Caspari and Stern (1948). Muller states on page 10 "A recent paper by Spencer and Stern….extends the principle (i.e., one-hit principle) down to total doses of 50 r and 25 r". In the next paragraph, he states: "It is true, in a parallel paper….Caspari and Stern have reported results somewhat deviating from the above." In footnote 1 on page 10 of the article cited above, Muller adds "Uphoff and Stern have published a report of further work, with doses as low as 50 r, given an intensity as low as 0.0165 r per minute. The results obtained are entirely in conformity with the one-hit principle. A consideration of these results, together with the early work, leads to the conclusion that the deviation first referred to (the Caspari and Stern (1948) findings) was caused by a value for spontaneous mutation rate that happened to be unusually high." Although this repeatedly false criticism by Muller was indeed highly disconcerting, other geneticists seemed too willing and ready to accept it, more or less on 'blind faith" and without proper review and verification. If they had chosen to follow the data originating from Muller himself (Muller, 1945) and his own graduate students (Byers, 1954; Byers and Muller, 1952) as well as others (Graf, 1972; Rinehart, 1969) then perhaps the findings of Caspari, and not of Uphoff, would have received public attention and support. Thus, Muller continued to perpetuate a false view that was discredited by his own statements/data. Shamefully, there is no evidence that anyone challenged Muller on these contradictions. Furthermore, Muller claimed that the research of Delta Uphoff and Curt Stern was "entirely in conformity with the one-hit principle" (Timoféeff-Ressovsky et al., 1935). What Muller neglected to state was that Uphoff's first two experiments displayed an aberrantly low control group responses based on Muller's own extensive data involving some 200,000 fruit flies (Muller, 1946). A letter from Curt Stern to Ernst Caspari (fall 1947) (American Philosophical Society, 1947a) addressed the control group issue. It states: "The radiation data continues to be puzzling. Delta's difference between control and exper[imental group] appears to be due mainly to a much lower control group value than yours. However, Muller informs me that this data give an aged control value close to yours. Thus, my first idea that your results could be "explained away" by assuming that your control value happened to be unusually high, seems unlikely. Rather does Delta's control appear too low". Muller's false and self-contradictory statements about Caspari's findings may be understood within the context of his ideological focus on establishing the LNT model for risk assessment and in the preservation of his legacy – a legacy that would have been severely tarnished if the deceptive remarks he made during his Nobel Prize Lecture had been discovered.

A further example of Muller's duplicity in promoting the LNT concept was his inaccurate characterization of the dose-rate used in the Uphoff experiments (Uphoff and Stern, 1949), which was 0.00165 r/min, i.e., 50 r in 30,240 min or in 21 days) (Uphoff and Stern, 1949). In his paper entitled "Radiation Damage to the Genetic Material" in the *American Scientist*, Muller (1950b) indicated that their research extended "the principle of proportionality of mutation to doses down to doses of 50 r and 25 r and of less than 0.001 r/min with a time–intensity relation differing by over 400,000 times from that of our high intensity dose." By using the incorrect dose-rate of <0.001 r/min (instead of 0.00165 r/min) Muller (1950b) extended the linear extrapolation over 400,000-fold, some 150,000-fold greater than what the correct dose-rate would have predicted. Just as in the case of validating the Uphoff control groups (discussed above), no one challenged Muller on this point. It is doubtful that Muller's actions was a simple editorial-typo as it involved two discrete changes, removing a 65 and adding a $<$ sign. Furthermore, Muller (1950b) had correctly cited the value as 0.00165 r/min in a previous paper.

4. The NAS BEAR I Committee Genetics Panel

The actions of Muller and Stern (cited above) were critical in persuading the radiation genetics community to adopt the LNT perspective, which was reinforced at multiple levels. By the early 1950s, according to Crow (1995), LNT had become the dominant

view of this group, despite having little support elsewhere. This timing is important as it set the stage for the actions of the NAS Genetics Panel on the Biological Effects of Atomic Radiation, which issued its landmark report on June 12, 1956, and published its technical report in the journal *Science* (Anonymous, 1956a) later that month.

Since the nature of the dose response in the low dose range was a critical issue, it would be important to know how the Genetics Panel debated this issue, what the nature of the debate was, what votes were taken on the general dose response issues, and who were the leading participants in the discussions. The Genetics Panel formally met on November 20 and 21, 1955, at Princeton University and on February 5 and 6, 1956, in Chicago. Transcripts were obtained for both of these meetings. The Panel had a follow up meeting March 1, 1956, with partial attendance and only a meeting summary (i.e., no transcript was taken). Intermeeting communications among Panel members were encouraged via the exchange of working documents and draft materials. These communications were typically preserved in the historical record, and it was generally possible to obtain copies of papers and correspondences of the Panel members on BEAR I from their respective institutional libraries. Although that which was archived varied according to each person, an effort was made to obtain complete sets of information on all Panel members. As a result, copious files on Panel members were obtained, enabling the reconstruction of Panel activity to a high degree.

The transcripts of the Genetics Panel indicate that the members debated neither the nature of the dose response at low doses, the expectations of a linear or a threshold dose response nor any other dosimetric issue. Dr. Tracy Sonneborn from the University of Indiana, a Panel member and colleague of Hermann Muller, wrote a general guiding statement of principles for the Panel to follow; see (Calabrese, 2015a) – Supplementary material. The basic framework consisted of four principles, i.e., that all doses of ionizing radiation were (1) harmful, (2) irreversible, (3) cumulative, and (4) displayed a linear dose–response relationship. No member of the Panel challenged these perspectives. In fact, at the Princeton meeting of the Genetics Panel, Professor Alfred H. Sturtevant from California Tech asserted his disdain for the medical profession that still adhered to an anachronistic belief in the threshold dose response model. Sturtevant stated that he had "no doubt about the correctness of the linear dose response" and that any effort to further document support for it would only be for the "propaganda value" needed to educate and convince the non-geneticists; see (National Academy of Sciences (NAS), 1955) – Transcription, November 21, 1955.

The Panel's single-minded uniformity of belief regarding the nature of the low-dose response was profoundly significant as it tended not only to limit discussion and preclude debate but also to ensure adoption of their preconceived notions. Due to this lack of discussion and absence of debate, the Panel was challenged to identify other activities that could productively fill its meeting times. The Panel Chair, Dr. Warren Weaver of the Rockefeller Foundation, forged ahead and challenged the 13 geneticists on the 17-member Panel to provide estimates of genetic damage to the U.S. adult population given a specific exposure to the gonads. The purpose of this exercise was to see how closely individual estimates of damage might converge among a blended mix of high level expert geneticists who had collective experiences studying an array of diverse populations, including fruit flies, bacteria, paramecia, yeast, human populations and clinical patients, among others. Weaver argued that a greater convergence (i.e., agreement) among individual damage estimates would tend to yield a greater confidence by society in the Panel's scientific conclusions and recommendations. Although one geneticist resigned from the Panel due to overriding academic commitments, the remaining 12 considered the challenge and the need to independently complete the assignment within about one month following the meeting of February 5–6, 1956. Of the 12 geneticists three (Tracy Sonneborn, Clarence C. Little and James V. Neel) eventually decided that there was too much uncertainty for the question to be quantitatively addressed with any degree of accuracy or reliability and that any population-based estimates would simply be misleading. For example, Neel stated that the scientific foundations needed to make such estimates of genetic damage were so uncertain that providing them would be a violation of his obligation to society as a scientist; see the April 6, 1956 letter from Neel to Weaver, cited in Jolly (2004). After the refusal of these three Panel members to participate in the exercise and provide estimates, the nine remaining geneticists may have had similar misgivings, at least to some extent, but nonetheless provided quantitative estimates of genetic damage within the prescribed time; see (Calabrese, 2015a) – Supplementary material.

When the Panel finally published its paper in *Science*, it indicated erroneously that six (instead of nine) geneticists took up the challenge and provided such estimates (i.e., "Six of the geneticists on this committee considered the ....problem."). This apparent discrepancy triggered a more extensive assessment of communications among panel members and related information regarding the estimates of damage. Chairman Weaver gave James Crow the task of organizing the submitted material and integrating tables listing the damage estimates of each participating geneticist. As a result of this process, it quickly emerged that there was considerable disagreement among Panel members concerning the identity and appropriate use of methods and assumptions in conducting the assignment. Thus, as one can imagine, confusion about the assignment and the lack of a clear protocol yielded estimates of extreme variability. Panel members were highly uncertain of their own estimates, which often radically disagreed with the estimates of fellow Panel members. In spite of the fact that each geneticist employed the linear dose–response assumption, the results of this exercise led to anything but a convergence. A close reading of all the contributions reveals that some of the "experts" had little idea how to approach the problem. This can be highlighted in the case of James Crow, the last surviving member of the Panel, who died in 2012. For example, on March 29, 1956, Crow stated (Crow, 1956): "I shall use as a minimum estimate a direct extrapolation from Drosophila and as a maximum some calculation from the sex-ratio in the Japanese cities. An estimate from mouse data turns out to be just about half way between these, so I shall use it as the most probably estimate." The non-sequiturs inherent in such biological reasoning demonstrate how poorly some of the leading experts addressed this issue. As the other geneticists expressed similar levels of uncertainty and disagreement, it is not surprising then that the Panel would share their documentation with neither external reviewers nor the interested public.

A major problem arose as a result of the extreme variability among the individual estimates. That is, the uncertainty of these estimates would erode public confidence in the Panel's pronouncements. Crow perceived the problem and memorialized his concern in a letter to Chairman Weaver of March 29, 1956: "The limits presented on our estimates of genetic damage are so wide that the reader will, I believe, not have any confidence in them at all." Thus, Crow believed that if the Panel shared its uncertainty with the public then the likelihood of winning their acceptance of any scientific and policy guidance would be seriously threatened. Crow then made a unilateral decision to exclude the estimates of three of the geneticists (i.e., Kaufmann, Wright and Demerec), the three with the lowest estimated damage values; see (Calabrese, 2015a) – Supplementary material for a detailed assessment for each of these three excluded values. Although Crow's decision

markedly reduced the amount of variation within the group, this initial "adjustment" was simply not enough to solve the variability problem. Crow then strongly urged the Panel not to share the six remaining and highly variable assessments with the scientific community and public. The Panel eventually voted on Crow's recommendation, and the majority decided in favor of it, thus essentially eliminating anyone from the interested public or the science community from critically examining the data or the process by which these estimates were derived. While a copy of the voting tally was obtained, specific information on votes of individual members was discovered for four members. Based on their preserved correspondence, (Calabrese, 2015a) – Supplementary material, Crow, Glass, Muller and Sonneborn all voted not to share the data.

The aforementioned analysis reveals that the Genetics Panel deliberately falsified the research record in the *Science* article by reporting that only six geneticists provided estimates of radiation induced genetic damage. This was patently false as nine geneticists provided detailed estimates within the prescribed period of time. There was no expectation and no established protocol for the exclusion of estimates as each geneticist on the Panel was considered an independent world-class expert in his own area of genetics. The person who excluded the three estimates was Crow, who lacked the authority to do so. In fact, the exercise on estimating risk of genetic damage was designed to develop a gage of expert agreement or lack thereof. Removing the three estimates was a deliberate act to obscure and mitigate the magnitude of disagreement and uncertainty that existed among the experts. Furthermore, the report did not even acknowledge that three other Panelists refused to participate in the exercise because too much uncertainty precluded the possibility of making any reliable estimates, (Calabrese, 2015a) – Supplementary material. Finally, the *Science* article contained an inaccurate estimate of response variability in the range of plus or minus ten-fold on either side of the mean. More specifically, the *Science* paper states, "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 100-fold uncertainty markedly misrepresented the range of uncertainty of the six remaining Panel geneticists for estimating the next generation, which had a mean uncertainty value of 756 (312.5 median). See Table 1 of identified individual values in Calabrese (2015a) – Supplementary material.

The Genetics Panel of the NAS, as a group, therefore deliberately sought to misrepresent the research record in their landmark *Science* publication on three distinct aspects. These included: the incorrect statement that only six geneticists provided genetic damage estimates when nine did; the failure to report that three other geneticists refused to provide any estimates at all because of the high level of uncertainty of this exercise; and, finally, the uncertainty range for the six geneticists was given as 100 fold when the mean value was actually 756 fold. These actions of fabrication and falsification by the Genetics Panel were undertaken to ensure that governmental agencies, legislative bodies and the general public would be more likely to accept the Panel's LNT-derived policy recommendations for assessing the risk of ionizing radiation.

5. BEAR I Genetics Panel report – fallout

Following its acts of falsification and fabrication of the research record, the Genetics Panel continued to show its arrogance in the aftermath of the BEAR I Panel and at the start of BEAR II (fall, 1956). In this case, several leading biologists had requested that the Genetics Panel provide documentation that would explain/support its decision to recommend the adoption of the linear dose–response model for risk assessment purposes, (Calabrese, 2015b) – Supplementary material and Glass (1956). The biologists noted that the BEAR I Panel had proclaimed the correctness of the LNT model, but it failed to provide any written scientific basis for its decision. Since providing documentation to support major decisions is the main mission of any NAS Committee, the BEAR I Genetics Panel, by this standard, clearly failed to perform its mission. However, in a decision that may be difficult to understand, the Panel actually refused to do so, deciding instead to redirect its efforts to identifying research areas for future funding. Furthermore, it is highly unusual, if not astonishing, that the Panel actually informed the President of the NAS, Detlev Bronk that it had decided not to provide documentation to support the LNT recommendation. In fact, no documentation in support of the LNT decision ever existed at the time of the BEAR I Genetics Panel report on June 12, 1956, and now it would have to be written well after the fact – a serious problem in and of itself. Secondly, the Panel members openly noted that they preferred to spend their time identifying research priorities for funding opportunities, some of which would be of interest to their own research laboratories. No evidence has been found to suggest that President Bronk ever objected to the Panel's no documentation decision, which was shared with him in a letter from George Beadle, Chair of the BEAR II, Genetics Panel (Beadle, 1957) on September 11, 1957. Thus, the President of the NAS was complicit in the decision not to require the BEAR Genetics Panel to document its support of the LNT model.

The BEAR I and II Panels consisted of essentially the same individuals except for two changes. The Chair (i.e., Warren Weaver) stepped down so he could award grants from the Rockefeller Foundation to Panel members without an obvious conflict of interest, and one new person (TG Dobzhansky) who had been invited for BEAR I, but was unavailable at the time.

The BEAR I, Genetics Panel released their report amongst a flurry of media attention with front page stories in the *New York Times* (Leviero, 1956) and *Washington Post* (Haseltine, 1956). Other leading venues, including *US New and World Report* (Anonymous, 1956b), *The Saturday Review* (Muller, 1956), *Time Magazine* (Anonymous, 1956c, 1956a), *Science* journal (Anonymous, 1956c), *The Lancet* (Anonymous, 1956f, 1956g) and others, also had articles on the BEAR I Genetics Panel report. The *New York Times* called it the most extensive study ever conducted by such a leading group of experts. Yet, in retrospect the evidence shows that the effort failed in critical ways, especially in not even debating the key question concerning the nature of the low dose zone in the dose–response paradigm. The Panel proclaimed the validity of the linear model at the start and never felt the need to justify this fundamental decision, even following a subsequent challenge by leading biologists. Such inappropriate actions of the Panel continued, as it even deemed it necessary to fabricate and falsify the record in their key *Science* publication to ensure that their views would be accepted. All this was clearly expressed in newly unearthed records of the Panel's correspondence. The dishonesty of the Panel was nothing new as it was simply carrying on a tradition seeded a decade earlier by Hermann J. Muller at his Nobel Prize Lecture.

The explicit deceptions of some Panel members continued even some 35 years after the fact. For example, Panel member and geneticist Bentley Glass (Glass, 1991), in a book review about the Rockefeller Foundation, retold the BEAR I, Genetics Panel story reported in the 1956 *Science* article concerning how the Panel obtained its estimates of genetic damage in the U.S. population. Glass wrote that Chairman Weaver sought to overcome vast disagreements among Panelists by instructing them to return to their hotel rooms and work out their damage calculations individually.

The following day, Glass reports, the disagreements were profoundly diminished and a strong consensus emerged. The story by Glass may well be how he remembered the event but his memory is strongly contradicted by the factual record. The fabrications of Glass started with his "authoritative" quote from Weaver that inspired the geneticists to return to their rooms. The quote does not exist in the meeting transcripts. The story of Weaver sending Panelists to their hotel rooms to work on their estimates and of their returning the next day in triumphal consensus likewise never occurred. In fact, Weaver charged them to return to their respective homes and gave them about a month to work on the estimates. Thus, once again, based on the transcripts and substantial subsequent written communications, Glass bears false witness. Glass's most significant fabrication is that the Panelists actually reached a strong quantitative agreement. The consensus story was not real but faked by Weaver and the Panel as discussed above and detailed elsewhere, (Calabrese, 2015a) – Supplementary material.

The highly regarded Glass, among whose honors included being a President of the AAAS and Phi Beta Kappa, amongst numerous other honors, repeated, therefore, the long established false narrative, reinforcing the LNT mantra well into the modern era of risk assessment and doing so with great appeal to his authority. This is therefore the story of not only how the U.S. and world governments came to adopt the linear dose response for risk assessment but also how its origins were forged by deception, artful dodges and blind faith to become established, preserved, protected and reinforced by those very people (e.g. Genetics Panelists) and organizations (e.g. NAS) that society is supposed to trust.

6. The Rockefeller Foundation and the LNT

In 1954, the Board of Trustees of the Rockefeller Foundation (RF) developed the proposition that it was necessary for the United States (U.S.) to undertake a major assessment of ionizing radiation on humans and the environment. One of their Board members was Dr. Detlev Bronk, who was also serving at that time as the President of the Rockefeller Institute for Medical Research (which would become Rockefeller University in 1965) and President of the U.S. National Academy of Sciences (NAS). Prior to this time, Dr. Bronk had also been the President of Johns Hopkins University and the President of the American Association for the Advancement of Science (AAAS) in 1952. Bronk took the proposal of the RF Board of Trustees to the NAS and received permission to undertake this project as an official NAS activity (Hamblin, 2007). This new project was called the NAS Biological Effects of Atomic Radiation (BEAR) Committee. The project involved six independent technical panels for different areas of concern (e.g., genetics, pathology, oceanography and fisheries, agriculture, meteorology, and waste disposal and dispersal). The panels were created by Dr. Bronk and administratively overseen by the RF.

All six BEAR Committee expert panels were chaired by renowned experts in their respective fields except for the Genetics Panel, which was chaired by Warren Weaver, a mathematician and long-time administrator at the RF (Rees, 1987). Interestingly, Bronk selected Weaver to chair the Genetics Panel and, as such, this selection represented a striking deviation in panel construction and leadership. Although multiple individuals with considerable relevant scientific expertise and strong leadership skills were already on the Genetics Panel, none of them would be selected as Chair. Overlooked in the selection process were: George Beadle, the future President of the University of Chicago (and 1958 Nobel Prize winner); Alexander Hollender, the highly regarded scientific administrator at Oak Ridge; Clarence C. Little, the past President of the Universities of Maine and Michigan; and Milislav Demerec, Head of Genetics at Cold Spring Harbor.

In the selection of panel members, one suspects that Bronk and Weaver may have intended to “stack the deck” with radiation geneticists who supported the LNT. For example, Ralph Singleton was a radiation geneticist at the Brookhaven National Laboratory who at the time, questioned the linearity hypothesis and reported a non-linear relationship between mutation rate and dose rate, with disproportional increases at higher doses (Singleton, 1954; Richter and Singleton, 1955; Sparrow and Singleton, 1953). In an April 17, 1955 article in the *New York Times,* (Anonymous, 1955b) Singleton challenged the linearity concept for genetic damage stating “there probably is a safe level of radiation, below which no genetic changes occur.” Singleton’s expertise and the timing and topic of his publications would seem to have easily qualified him for membership on the Genetics Panel, assuming of course that the key objective was to form a panel representing diverse viewpoints to encourage discussion and thoughtful consideration. As it turns out, Singleton was not appointed to the Genetics Panel but to the Agriculture Panel of BEAR I.

The BEAR Panels were the creation of the RF, fully funded by the RF, administered by RF staff and directed by a member of the RF Board of Trustees, who was also President of the NAS. Not only did Dr. Bronk help to conceptualize the project, but he was also part of the organization that funded the project and led the organization that received the funding and oversaw the project, including guiding the selection of panel chairs and their members.

For a long time, the RF was a major funding organization for radiation geneticists, including members of the Genetics Panel. The funding of such members extended over three decades, much of which was during the employment of Weaver and also under his direction. As noted in Wynchank (2011) and prior to the creation of the Genetics Panel, the RF had funded nearly four million dollars to the University of Indiana for research in the area of radiation genetics alone. Such funding supported the research activities of Professors Sonneborn and Muller, both members of the BEAR Genetics Panel.

Weaver was clearly aware of the importance of RF funding to radiation geneticists and showed no reluctance in connecting the Panel’s success to opportunities of lavish funding for its members. Weaver specifically stated at the February 5, 1956 meeting of the Genetics Panel that he would "try to get a very substantial amount of free support for genetics if at the end of this thing we have a real case for it. I am not talking about a few thousand dollars, gentlemen. I am talking about a substantial amount of flexible and free support to geneticists”, (National Academy of Sciences (NAS)/National Research Council (NRC), 1956) – NAS transcripts, February 5, page 35. As part of his interaction with the Genetics Panel, he prefaced his funding remarks with the statement that "There may be some very practical results – and here is the dangerous remark – don't misunderstand me. We are just all conspirators here together." The remarks of Weaver were blunt and remarkably focused linking the project outcome to the funding interests of the geneticists on the Panel. Such a blatant coupling of funds and outcome were highly manipulative.

Could such an inducement, as grant support, really be persuasive enough to affect the performance, judgment or integrity of esteemed scientists on an NAS Panel? In his 2007 dissertation (Seltzer, 2007), Seltzer sheds some light on this question. He concluded that members of the Genetics Panel saw themselves as funding advocates for radiation genetics (p. 285 footnote 208). Furthermore, it was hoped that the Genetics Panel, which would continue into the foreseeable future, would affect the directions and priorities of funded research in genetics. Seltzer (2007) also further showed that such expectations were in fact evidenced in correspondence between members of the Genetics Panel, i.e.,

Beadle, Dobzhansky, Muller and Demerec. In a letter to Beadle, Demerec (American Philosophical Society, 1957a) offered a funding plan that could be achieved by "setting aside a fund (let us say, one hundred million dollars), to be administered by some competent organization (such as the National Academy of Sciences) and used during a period of 20 or 25 years to fund already functioning research centers so as to attract and train first rate scientists". Dobzhansky (American Philosophical Society, 1957b) responded to this proposal by stating that he would "needless to say, be all in favor (of) $100,000,000 for research in general genetics…. but I would find it hard to keep a straight face arguing that they (general genetics) must be studied to evaluate the genetic effects of radiation on human populations". This evoked from Demerec (American Philosophical Society, 1957c) the statement that "I, myself, have a hard time keeping a straight face when the talk is about genetic deaths and the tremendous dangers of irradiation. I know that a number of very prominent geneticists, and people whose opinions you value highly, agree with me". Finally, Dobzhansky (American Philosophical Society, 1957d) responded by saying "Let us be honest with ourselves – we are both interested in genetics research, and for the sake of it, we are willing to stretch a point when necessary. But let us not stretch it to the breaking point! Overstatements are sometimes dangerous since they result in their opposites when they approach the levels of absurdity. Now, the business of genetic effects of atomic energy has produced a public scare, and a consequent interest in and recognition of (the) importance of genetics. This is to the good, since it will make some people read up on genetics who would not have done so otherwise, and it can lead to the powers-that-be giving money for genetic research which they would not give otherwise" (American Philosophical Society, 1957d).

These shared comments by key members of the Genetics Panel provide previously unknown insights into motivations of the leading radiation geneticists of that era and the group that legitimized LNT for use by society. According to Seltzer (2007), these letters made two points: (1) that the geneticists were quite focused on the viability of their discipline and (2) that they were cognizant of and acted upon opportunities to manipulate the current situation (e.g., to stretch a point) for the purpose of increasing the likelihood of greater funding. It seems as though the persuasiveness of grant funding is more powerful than one could have imagined, even for esteemed scientists.

When viewed from a grander perspective, the RF displayed an undue and unheard of influence over the course of cancer risk assessment within the United States and throughout the world. The RF directed and funded the entire process that resulted in the adoption of the LNT, all hidden within the prestige of the U.S. NAS due to the multiplicity of roles played by Bronk. Weaver used his long-honed knowledge and skills concerning the vulnerability of academics for external grant funding and lured Panel members with funding possibilities on the basis that their area would be seen as important to society. Such manipulations raise serious ethical issues. In fact they paved the way for the very activities that occurred within the Genetics Panel, that is, misrepresenting the research record to enhance its policy recommendations. To ensure a "proper" narrative, Weaver the mathematician, and not one of the geneticists, drafted the final report of the Genetics Panel (Glass, 1991). At an organizational level, the RF manifested hegemony over the BEAR Genetics Panel, warping and corrupting a risk assessment process that had lasting, social and economic public policy consequences. At an individual level, Bronk's failure to require the panel to document the scientific basis for the LNT recommendation and the Panel members' self-serving decision to identify funding opportunities instead of writing the report, together represent unscrupulous behaviors that enabled them to establish the legitimacy of the LNT model without having to defend their position and, at the same time, optimizing their future funding options.

7. Conclusions

- The recommendation by the U.S. NAS in 1956 to adopt the LNT model was rapidly accepted by governments worldwide and provided the basis for estimating cancer risks from ionizing radiation and chemical carcinogens over the past six decades.
- The recommendations of the U.S. NAS BEAR I Committee, Genetics Panel were ideologically-driven with no written scientific basis provided by the Panel.The Genetics Panel explicitly refused to provide a written documentation when formally challenged to explain their recommendations. Moreover, the President of the NAS became complicit in the Panel's questionable and irregular actions by taking no corrective action, even after receiving notification by letter of the Panel's refusal to provide such a report.
- Studies under the direction of Curt Stern at the University of Rochester/University of California-Berkley using Drosophila provided the scientific basis for the LNT of the BEAR I Genetics Panel. Detailed re-analyses of these studies has revealed serious flaws in the acute study by Warren Spencer and in key follow up chronic exposure experiments by Delta Uphoff. Curt Stern intentionally concealed critical limitations of the Uphoff findings which had Stern and Uphoff characterize these findings as "uninterpretable". Stern, in cooperation with Hermann Muller, deliberately misrepresented and marginalized the findings of Ernst Caspari which supported a threshold model.
- The NAS Genetics Panel committed scientific misconduct by falsifying, fabricating and then publishing in the journal Science its doctored estimates of human genetic risk to radiation exposures. The Panel's deceits were designed to prevent the scientific community and the general public from knowing the profound uncertainties entailed in its genetic risk estimates, thereby insuring the ready acceptance of its policy recommendations.
- Current cancer risk assessment policy and practices are based on fraud and deception by key leaders of the radiation geneticist community and by the U.S. NAS, BEAR I, Genetics Panel. Their deceptions were uncritically adopted by regulatory agencies and the scientific community worldwide and provide the foundation of cancer risk assessment and risk communication messages. The implications of such fraudulent actions are profound and likely to affect: human health risk assessment, adoption and use of new technologies, cost benefit assessments at multiple societal levels, toxic tort actions/decisions, and in the education of the public on vast areas of environmental health and medical treatment practices.

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LETTER TO THE EDITOR, NEWS AND VIEWS

An abuse of risk assessment: how regulatory agencies improperly adopted LNT for cancer risk assessment

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Abstract The Genetics Panel of the National Academy of Sciences' Committee on Biological Effects of Atomic Radiation (BEAR) recommended the adoption of the linear dose–response model in 1956, abandoning the threshold dose–response for genetic risk assessments. This recommendation was quickly generalized to include somatic cells for cancer risk assessment and later was instrumental in the adoption of linearity for carcinogen risk assessment by the Environmental Protection Agency. The Genetics Panel failed to provide any scientific assessment to support this recommendation and refused to do so when later challenged by other leading scientists. Thus, the linearity model used in cancer risk assessment was based on ideology rather than science and originated with the recommendation of the NAS BEAR Committee Genetics Panel. Historical documentation in support of these conclusions is provided in the transcripts of the Panel meetings and in previously unexamined correspondence among Panel members.

Keywords Mutation · Linear non-threshold (LNT) · Risk assessment · Carcinogen · Threshold dose response · Ionizing radiation

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The most significant event in the history of environmental risk assessment was the recommendation by the United States National Academy of Sciences (NAS), Biological Effects of Atomic Radiation (BEAR) Committee, Genetics Panel in 1956 to switch from a threshold to a linear dose–response model for the assessment of genomic mutation risk (Anonymous 1956; NAS/NRC 1956). Within a brief period of time, this recommendation became generalized to somatic cells by other governmental advisory committees and was eventually applied to cancer risk assessment. Although this linear dose–response paradigm was originally intended to be used for ionizing radiation, it would later be adopted by the US Environmental Protection Agency and directly applied to chemical carcinogens (Albert 1994; Calabrese 2013a, b), thereby affecting worldwide cancer risk assessment for the past several decades.

Given the significance of this action by the NAS BEAR I Committee, Genetics Panel and the long history of the threshold dose–response model in regulatory practice, I was interested in learning the answers to several key questions: how was this recommendation made, what was the nature of the debate, what were the persuasive and compelling arguments, and what were the roles played by various individuals on the Panel? I therefore obtained transcripts of the BEAR I Committee, Genetics Panel meetings in 1955 and 1956. It was a bit like reading the book after seeing the end of the movie. To my surprise, the BEAR I Committee, Genetics Panel was uniformly confident in their belief that linearity for genomic risk assessment was the correct perspective, while being arrogantly dismissive of both the threshold perspective and those who supported it. So dismissive of the alternative model was the Genetics Panel that it was never viewed as a debatable issue, nor was it ever debated. What a disappointment. I had so looked forward to retrospectively witnessing how the leading thinkers of

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their time confronted this seminal issue on dose–response, how they intellectually sparred with one another, and whose logic and facts helped carry the day for the linearity model. The NAS BEAR I Committee, Genetics Panel made the switch from a threshold to a linear dose–response risk assessment model by "proclamation," with no debate and without providing a detailed (or actually even any) evaluation, such as would be expected of any scientific advisory group—most certainly of one at the level of the National Academy of Sciences on such matters of national and international significance. In retrospect, this should not have been too surprising as I had documented in previous publications (Calabrese 2011a, b, 2012, 2013a, b) the inherent intellectual dishonesty of key leaders of the radiation genetics community, such as Curt Stern and Hermann Muller on the issue of threshold versus linear dose–response and how they successfully distorted the scientific record in order to achieve their goal of a linear dose–response for risk assessment. The linear dose–response recommendation by this Genetics Panel would be broadly extolled by leading media outlets on the day of its release as the most extensive assessment ever undertaken on the topic by a most prestigious group of American scientists. The National Academy of Sciences report was literally a front-page story in the New York Times with the linearity risk assessment framework leading the way.

Despite the widely acknowledged success of the BEAR I Committee, Genetics Panel in getting their message out to the scientific community, governmental bodies, and the public, the reports of the BEAR I Committee, Genetics Panel were eventually read by members of the scientific community. This resulted in a number of leading biologists challenging the Genetics Panel, demanding to know the scientific basis of the decision in favor of linearity. However, as noted above, the Genetics Panel had not undertaken such an assessment and was not in a position to explain their actions nor to defend a report that lacked a scientific foundation. Showing its disdain for those challenging this report, the Genetics Panel decided not to provide the information to the scientific community. This decision was rendered to the President of the National Academy of Sciences without any evidence of his objection. The adoption of the linear non-threshold (LNT) dose–response model by the National Academy of Sciences therefore was made without a scientific assessment and, of course, a refusal to provide one when challenged.

The recommendation to switch to a linear dose–response by the NAS BEAR I Committee, Genetics Panel, as announced to the world by leading media outlets, reflects an abdication of societal responsibility on a critical and enduring public health issue. This paper provides the first reporting of these actions in the history of the National Academy of Sciences and in governmental risk assessment practices for cancer. It reveals that current cancer risk assessment practices originated from an ideological set of beliefs from leading scientists rather than a scientific assessment. A fully documented assessment of this story is provided in the Supplementary Data section.

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Supplementary Material

LNT'S FAILED HISTORY:
An Abdicated Responsibility - How the US NAS BEAR I Committee Genetics Panel Failed To Assess LNT Prior To Recommending Its Use by US Regulatory Agencies

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Abstract

The U.S. National Academy of Sciences (NAS) Biological Effects of Atomic Radiation (BEAR) I Genetics Panel report recommended a linear dose response to assess the risk of genomic mutation from ionizing radiation. This represented a major change assessing risks which had been based on a threshold dose response model. This recommendation was soon generalized to somatic injury and applied to cancer risk assessment for ionizing radiation and later for chemical carcinogens. An evaluation of the transcriptional records of the Genetics Panel, intra-panel correspondence and work products, reveals that the Panel failed to provide an assessment of which dose response model best characterized the effects of ionizing radiation on the genome. Lacking such an assessment, the recommendation for a linear model was based upon an assumption of the Panel.

The Panel's failure to assess the scientific basis of the dose response for ionizing radiation, while recommending strongly a switch to linearity, represents an abdication of responsibility. It led to a deliberately false public understanding that their risk assessment for ionizing radiation was based on "the most comprehensive effort" ever undertaken in the United States by a committee of outstanding scientists as characterized by a front page New York Times story (Leviero 1956) one day after the release of the Panel report (June 13, 1956) and similarly reported in other scientific and public venues.

Key Words: linearity, threshold, mutation, risk assessment, dose response, cancer

Introduction

The US NAS BEAR I Committee Genetics Panel in 1956 recommended that the risks associated with ionizing radiation to the human genome no longer be evaluated via the use of a threshold dose response model but with a linear at low dose model. This recommendation was quickly adopted by the scientific and regulatory communities and soon generalized to somatic cells for application to cancer risk assessment for ionizing radiation (Taylor 1960, 1963, 1965). Some two decades later the U.S. NAS Safe Drinking Water Committee (NAS 1977) relied upon this linearity at low dose recommendation for assessing risks of chemical carcinogens. In many respects, therefore, the report of the 1956 BEAR I Genetics Panel was the most influential advisory report ever published on risk assessment. The Genetics Panel published two reports, one as part of a general NAS document intended for the media and the general public (NAS/NRC 1956), while the other was a more technical paper published in the journal Science (Anonymous 1956a). The key conceptual conclusion of the Genetics Panel was that ionizing radiation induces genomic mutations which are nearly always harmful and the damage is irreversible, cumulative, and directly proportional to dose, such that there is no safe level of exposure.

NAS Genetics Panel

Since the toxicology, medical and regulatory communities were still being dominated by the threshold dose response model for all endpoints during this time period, the rejection of threshold dose response and its replacement with the linear model constituted no less than a major scientific and regulatory revolution. As such, one would expect that a principal task of the Panel was to document the strengths and limitations of the threshold and linearity dose response models and thoroughly debate this topic during their sessions prior to recommending the retention of the threshold model for genetic risk assessment, a switch to linearity or some other risk assessment approach. In anticipation of reading such an historic debate, yet knowing in advance that the Genetics Panel recommended the rejection of the threshold model and the immediate transition to linearity, the transcripts of the Genetics Panel meetings were obtained from the US NAS Archives. I was surprised to learn that the Panel did not research, assess, nor debate the dose response question. The issue of dose response risk assessment model selection had been "decided" by the closely knit radiation genetics community prior to the creation of the Panel, based on the leadership of Hermann J. Muller and Curt Stern [Calabrese 2013; Crow 1995). In fact, at the first meeting of the Genetics Panel on November 21, 1955 at Princeton University, the well-known geneticist Alfred Sturtevant from California Technical Institute was dismissive of the issue of dose response as he had "no doubt about the correctness of the linear dose response" model and that any effort to further document support for it would only be for "propaganda value," as means to educate and convince the non-geneticists. This dismissive, and indeed arrogant attitude, was pervasive amongst the geneticists on the Panel concerning their unique professional insights on the issue of mutation. In line with this perspective, the key leaders of the genetics community ascribed to a series of firmly held beliefs about radiation and mutations. In fact, at the second meeting of the Panel (February 5, 1956) Tracy Sonneborn, a member of the Panel and colleague of Muller at the University of Indiana, read into the record what amounted to a detailed series of "beliefs", in essence, a geneticist's creed, about dose response, mutation, ionizing radiation and risk assessment (starting on page 81 of the transcript) (i.e. nearly always harmful, irreversible, cumulative and linear) (NAS 1956). Amongst the Panel of 17 members, of which 13 were prominent geneticists, there was no dissent.

The "Debate"

The only attempt at "dissent" was initiated by Bentley Glass on February 5, 1956 (page 108 of the transcript) (NAS 1956). Glass stated that the only challenge to their geneticist creed as articulated by Sonneborn, to which he was aware, concerned the concept of linearity. Glass stated he wanted to explore the question (i.e., the challenge to linearity) within the Panel, "not because I believe personally in the objection that I am going to raise but to play the role of the devil's advocate here." What follows next is the transcript discussion immediately after the comment of Glass:

"DR. CROW: Which assumptions are these?

DR. GLASS: Well, they were in Dr. Weaver's formation too, but they are the two at the beginning of Sonneborn's genetic considerations.

After having made a talk to the physicists at Rutger's recently on this general topic of "The Geneticist Views the Dangers from Atomic Radiations," I was surprised to find that one of the geneticists who dained to come out to hear the talk challenged this particular assumption which I had put out as one of the assumptions that all geneticists are agreed upon, and his line of reasoning – which, of course, is something that the physicists will very eagerly and quickly seize upon I think because most of them want to believe in a threshold effect as at least a possibility, if not demonstrated beyond all question at the moment – his line of reasoning was as follows: that the view that there is no threshold in the response of mutations to dosage is largely based, apart from the experimental data, on the target theory of the effects of radiation, and that the microbial geneticists (and this man was a microbial geneticist) having shown that there is a chemical and indirect mediation between the production of ionizations and the

occurrence of point mutations makes it altogether probable that somewhere or other there is a threshold, and he felt very uncomfortable about the assumption that there is no threshold if you go down to low enough doses. This is heresy in their midst.
DR. WRIGHT: In energy if not in ionization. Isn't your threshold there in energy? Perhaps one electron volt or two does account for the threshold. But ionization is so far above any possible threshold that it does not seem to me that bears on the ionization argument at all.
DR. STURTEVANT: I have met with this objection. They have usually been willing to agree, however, if I worded it that at the moment the best bet is that there is no threshold and we have to proceed on that.
DR. GLASS: That is all right. But I think we have to take some cognizance of this argument.
DR. CROW: Do you know for certain in any area?
DR. WRIGHT: Isn't the experimental evidence practically conclusive there, to the extent that they have been spaced so that from the physicist's standpoint there is no possibility?
DR. CROW: If you have one ionization per hour or whatever.
DR. GLASS: It is convincing me, too.
DR. RUSSELL: There is both the theoretical and the practical viewpoint they have these several orders of magnitude from all the other kinds of things that we are questioning and recommending research on."

Chairman Weaver then refocused the discussion by inviting Panel member Bernard Kaufmann to discuss research of Arnold H. Sparrow from Brookhaven National Laboratory on mutations in plants at low doses. Kaufmann stated that Sparrow and Singleton (Sparrow and Singleton 1953) reported that 0.41 r per day gives a statistically significant mutation effect. Kaufmann failed to note that (on the top of Sparrow & Singleton's page 37) there was actually mutation data for a dose (0.084 r/day) lower than 0.41 r/day and that it had no treatment effect. This finding would have challenged the linearity position if it had not been omitted by Kaufmann. The page 37 statement of Sparrow and Singleton (1953) is as follows:

> "The data in table 2 show that 0.084 r per day caused no significant increase but that 0.41 r per day (or higher) did show a statistically significant effect (table 2). However, the increase was less than twice that of the control. Since 0.41 r per day of radiation is more than one thousand times greater than the naturally occurring intensity these data do not support the theory that the spontaneously occurring micronuclei are produced by naturally occurring ionizing radiation."

After the brief discussion of the Sparrow data and the misrepresentation of his data by Kaufmann all discussion on the issue of linearity vs threshold ended for the BEAR I Genetics Panel.

It is difficult to comprehend that this was the extent to which the Genetics Panel acknowledged the dose-response controversy and discussed the key scientific issues concerning the nature of the dose-response in the low dose zone. This had been a matter of contention for the past two decades with various high level advisory committees in the US and internationally. It was also a critical component of Muller's Nobel Prize lecture (Calabrese 2011a, 2012) and a major component of the health effects research of the Manhattan Project (Calabrese 2012, 2013; Caspari and Stern 1948; Spencer and Stern 1948; Uphoff and Stern 1949) and of the Atomic Energy Commission. In many respects, the principal reason for the creation of the Genetics Panel was to address the issue of how to assess genetic risks at low doses of ionizing radiation. In the end, the Panel provided the scientific community and the public with a statement of beliefs, none of which was researched, documented, assessed, debated and refined as might be expected if a legitimate evaluation process had been followed.

Acknowledgement of the BEAR I Genetics Panel Failure

On November 26, 1956 Bentley Glass wrote to the BEAR II Genetics Panel stating:
"From impressions I have gathered during the course of the past five and a half months since our report [BEAR I Genetics Panel Report] was released to the public [i.e., June 12, 1956], I have come to the

conclusion that there are several matters of some urging for consideration by our Committee." The second of these considerations related to the linearity question as now stated by Glass:

> "II. I have met continuing doubt from well-informed biological scientists in regard to the geneticists' assumption that there is no threshold for mutation. This leads me to believe that there is a need to prepare a statement and exposition of this point that will (A) summarize existing data on the matter, (B) present the physical arguments against the existence of a threshold, and (C) deal with the experimental possibilities of further investigating the question in suitable biological material."

The statement of Glass is significant in light of the report of the Genetics Panel in Science (Anonymous 1956a). It is clear that he received significant push-back to the LNT assumption by some "well informed biologists" such that he now felt it was necessary for the new Genetics Panel (i.e., BEAR II) to provide documentation in support of linearity and against threshold. Now that the Panel's report was challenged, Glass felt the need for an appropriate scientific response. Even in the case of Glass, his written statement indicates bias as he recommends not a search for scientific understanding of the nature of the dose response in the low dose zone for ionizing radiation, but how to make the case for linearity and against threshold. Based on such insights into the actions of NAS BEAR I Genetics Panel, this group was selected based on both high achievement and their unified belief that genetic mutations were considered irreversible, cumulative and linear with respect to dose. So strong was their collective belief that the group failed to provide any scientific justification for their highly influential linear dose response recommendation. Despite this suggestion by Glass now nearly six months after the release of the report, there was no demonstrable attempt to address this most fundamental issue, but rather their first item on the BEAR II Genetics Panel agenda was to propose a funded research program for the genetics community (Memo to Members of the Academy Genetic Committee - i.e., BEAR II) (Beadle 1956a).

This challenge of Glass (1956) would be a continuing one (August 24, Beadle Memo to Genetics Panel) (Beadle 1956b) for the Genetics Panel, even proceeding the letter of Glass (1956) and a finalizing of their internal debate based on a September 11, 1957 letter from the Chairman of BEAR II Genetics Panel (G. Beadle) (Beadle 1957) to Detlev Brock, President of the NAS and copies to Weaver (Chairman of BEAR I Genetics Panel) and the Panel. In this September 11, 1957 letter, Beadle stated that the development of a detailed technical document that would provide the scientific basis for the BEAR I Genetics Panel report was not justified since it would require excessive resources (i.e. one or two geneticists working full time), and there did not appear to be mounting external pressure to do so. Beadle then offered the incomprehensible suggestion that since several published review papers (none were identified) that presumably included some topics addressed in some manner by the Panel, there was no need to consider this issue further. Thus, the request of Glass was finally tabled, and the NAS leadership was fully informed of this decision.

Discussion

So what do these historical insights mean? The switch from threshold to linearity for risk assessment by the US and other governments that followed the NAS report was not based on an assessment of the issue, but rather on a set of pre-conceived beliefs. As demonstrated in a series of previous articles (Calabrese 2011a,b, 2012), these beliefs had been acquired via deliberate misrepresentation of the scientific literature by key leaders of the radiation genetics community, led by the Nobel Prize winner H.J. Muller and Curt Stern (Calabrese 2011b, 2013). It is apparent that the NAS administration, the scientific community and regulatory agencies failed to demand that the Genetics Panel provide a scientifically supported basis for their recommendation of a switch to the linear dose response.

A strong indicator of their public success became evident almost immediately when the New York Times (Leviero 1956) provided a front page story on June 13, 1956 with the title "Scientists Term Radiation A Peril to Future of Man: Even Small Doses Can Prove Harmful to Descendents of Victim". The first paragraph of the article stated that "A committee of outstanding scientists reported today that atomic radiation, no matter how small the dose, harms not only the person receiving it but also all his descendents." The next paragraph would claim that "it was the most comprehensive United States effort to determine how the future of the human race might be affected by the unleashing of nuclear power." Similar reports were also found in the Washington Post (Haseltine 1956), Time Magazine (Anonymous 1956b,c), US News and World Report (Anonymous 1956d), News of Science Section, Science journal (Anonymous 1956e), The Saturday Review (Muller 1956), Challenge Interviews (Weaver 1956), Journal of The Franklin Institute (Weaver 1957a), Bulletin of Atomic Scientists (Weaver 1957b), Public Health Reports (Weaver 1957c), Scientific American (Crow 1959; Beadle 1959), The Lancet (Anonymous 1956f,g) and other leading publications.

As the present paper demonstrates, the Genetics Panel's effort was anything but comprehensive. Rather, it represented an abdication of professional and ethical responsibility, using their outstanding reputations to present a false image of a detailed and objective assessment when it was their ideology that prevailed. While previous articles have captured Muller and Stern's scientific deceptions on the issue of linearity and their impact on the Genetics Panel (Calabrese 2013), and several members of the Panel in serious self-serving comments that undercut the credibility of the Panel (Calabrese 2014), the present paper has captured their silence and illusion as far as an effort to assess the nature of the dose response in the low dose zone.

Policy should be based on facts, not assumptions. In the absence of a factual foundation, the assumptions should be stated, explained, and justified. Not only did the Genetics Panel fail to serve the public, it was permitted to mislead US national policy and cancer risk assessment predictions and that of other countries by a compliant NAS administration, scientific community and press, under the false impression that their recommendation represented an objective and comprehensive assessment. The implications of this deception have been enormous and continue to the present.

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