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The Genetic Hazards of Nuclear Radiations

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Since the years 1927 and 1928, when Hermann J. Muller (*1*) and Lewis J. Stadler (*2*) independently discovered that x-rays will produce permanent hereditary alterations in animals and plants, respectively, the induction of mutations by ionizing radiations and the study of the changes brought about has become a major subscience of genetics. Hundreds of investigators have contributed to our present knowledge of radiation-induced mutation, and the full gamut of organisms, from viruses to flowering plants and mammals, has been found to be similarly susceptible. Meanwhile, great advances were also made in the cytological and biochemical analyses of the hereditary material, and today these approaches to an understanding of the intrinsic nature of mutations have come to a common focus. Our major question may then be phrased: How does radiation bring about permanent alterations of the hereditary material, and what kinds of changes are induced?

Chemical Nature of Hereditary Material

According to the overwhelming weight of present evidence, genetic information is transmitted from generation to generation in all organisms, sexual and asexual alike, through the chemical medium of deoxyribose nucleic acid or, in certain viruses, by another form of nucleic acid. The chromosomes, which have been demonstrated by genetic experiments to carry the units of heredity, the genes, are made up chiefly of deoxyribose nucleic acid and a basic protein, commonly a histone, together with some ribose nucleic acid and a small amount of nonbasic protein. The ribose nucleic acid, which is even more abundant in the nucleolus and the cytoplasm of cells than in the chromosomes, is thought to convey the chemically coded information from the nucleus to the sites of protein synthesis in the cytoplasm; but, except in certain viruses, it can hardly constitute the primary code itself.

Protein used to be thought the only substance of sufficient chemical complexity to be able to serve as the basis of heredity; but the advancing knowledge of the nucleic acids has revealed that they are equally capable of forming a virtually illimitable chemical code of information, through variations in the sequence of the four organic bases found in each polynucleotide; and the fact that the histone of the chromosomes in some species becomes completely replaced in the spermatozoa by an even simpler, more basic protamine seems to exclude the possibility that the protein of the chromosomes is the primary hereditary material. The evidence that the hereditary characteristics of *Pneumococcus* strains may be permanently transformed by subjecting recipient cells to the highly purified, extracted deoxyribose nucleic acid from donor cells of a different type, together with reconstitution experiments with tobacco mosaic virus, lend overwhelming weight to the view that nucleic acid, and generally deoxyribose nucleic acid, is the primary hereditary material.

In these reconstitution experiments, performed by Fraenkel-Conrat and others, the ribose nucleic acid core of one species of virus has been reenclosed in the protein coat of another. In each case, the infectivity and virtually all other hereditary properties of the reconstituted virus are those characteristic of the species that supplied its ribose nucleic acid, and not those of the species that supplied its protein (*3*).

We thus arrive at the view that the two purines of deoxyribose nucleic acid (adenine and guanine) and the two pyrimidines (thymine and cytosine) must in their seriation along the polynucleotide spell out the hereditary code, for the backbone of the polynucleotide, composed of deoxyribose units linked by phosphate groups to form a long chain, is similar in chemical structure throughout the length of the molecule. It is still quite uncertain how many nucleotides commonly comprise a gene, and whether the genes are separated by protein material or metal-ion bonds, or whether the genes are contiguous, or even overlap. But one must begin to think of mutations, at any rate, in terms of the chemical nature of the hereditary material and its sequences of bases. A mutation is some alteration in this material which, when chromosomes reproduce themselves, is itself replicated, and thus is transmissible in mitotic and meiotic cell divisions.

Chromosomal Mutations

Genetically detected mutations following exposure to ionizing radiations may involve microscopically visible alterations of the chromosomes or may be submicroscopic in character. The gross chromosomal aberrations, as is well known, include reciprocal shifts of segments between chromosomes, inversions of segments within a single chromosome, deficiencies arising by deletion of a segment, and duplications of a segment. In all these types of chromosomal mutation, it is easy to see that chromosomes have been fractured by the radiation and that their broken ends have been reunited in some new pattern. In each case, at least two breaks must have occurred within the same nucleus in order to permit the

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rearrangement, and it is therefore not surprising to learn that the frequency of such mutations increases as the square, or some higher power, of the dose.

At low dosages, such mutations are therefore very rare, since they involve the coincidence of two or more effective "hits" within the same nucleus. True, there are also single breaks which invariably lead to the loss of terminal parts of chromosomes, in case they do not heal together again (that is, "restitute"). But these, like the internal deficiencies, are invariably very harmful unless they are extremely small, at the lower limit of cytological visibility. They are consequently rapidly eliminated after a few cell generations or can only be kept for experimental study by great effort and ingenuity. They are, in other words, of a dominant lethal nature.

Translocations (except in certain plant species) may be described as commonly semisterile in effect; often they lower the viability of their carriers as well. Only the inversions and smaller duplications are in general sufficiently harmless to be transmitted in natural populations and to play a part in the evolutionary changes of species (*4*).

It is a striking fact that, in animals which have been used for studies of radiation-induced mutation, the male germ cells during meiosis, and especially during spermiogenesis, seem far more sensitive to the radiation than immature male germ cells (spermatogonia) or female germ cells of any stage (*5*). Inasmuch as the chromosomal mutations are produced chiefly by high doses, and in those very cells that are most readily eliminated through the production of the well-known temporary sterilization of the male after acute doses of radiation, there is relatively little genetic damage to be expected from them.

Point Mutations

Of chief importance, then, are the point mutations, in which the lesions in the hereditary material are submicroscopic in size. Submicroscopic mutations must be basically of a similar nature to the gross, cytologically visible mutations —that is, they presumably consist of alterations in the sequence of purine and pyrimidine bases, through inversions of segments, insertions, deletions, and substitutions.

All existing genetic evidence indicates that the frequency of point mutations increases linearly with the radiation dosage (Fig. 1). In studies of *Drosophila*, this has been demonstrated to hold over the dose range from 25 up to 6000 roentgens (*6*). In some plants, the linear range has been extended down to about 5 roentgens. In mice, the linearity in relation to dose holds over the range from 300 to 600 roentgens, but there is no sign that it does not hold below that range (*7*).

This linear proportionality to the dose, over and above the spontaneous frequency of mutation, implies two things: (i) as long as dosage is measured in terms of roentgens (that is, in terms of the ionization produced by the radiation) absorbed quanta are individually effective, and it does not take two or more to produce a mutation; and (ii) there is no sign of a threshold dose below which mutations are not produced, but rather, even the lowest doses are proportionally mutagenic, and all doses, however distributed, are additive or cumulative in effect. It also follows that, under normal conditions, the intensity with which the dose is given, whether in a short time at high intensity or over a long period at low intensity, whether given uninterruptedly or in fractions separated by rest periods, makes no difference.

Finally, these relations are also borne out by the evidence that differences in the energy of quanta are not significant with respect to mutation. Whether the quanta are the extremely powerful ones of cosmic rays or the less energetic ones of gamma radiation or x-rays, down to the weakest ionizing quanta of the grenz-rays, the mutational effect remains linearly proportional to the ionization produced. Ionizing particles, such as beta-rays (electrons), alpha-particles, and neutrons are also effective in producing mutations, both of the chromosomal and of the submicroscopic sort. They show differences in efficiency because of the differences in the ion density along the tracks of the various types of particles and consequently the differences in probability that one particle may produce more than a single lesion in a chromosome; but the dosage relation for the point mutations is in each case one of linear proportionality.

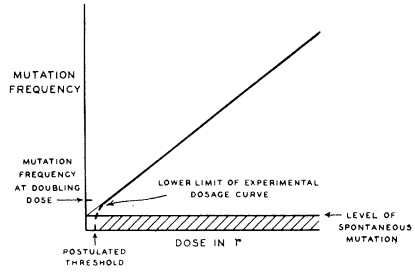

Fig. 1. Diagram to represent the relationship between mutation frequency and man-made dose of ionizing radiation. Note that the mutation frequency at the doubling dose is by definition double the frequency of spontaneous mutation. If a threshold existed below the lower limit of the experimentally demonstrated linear portion of the dosage curve, the curve would have to follow the heavy dotted line. This would imply that the lowest applied doses produced no mutations, and then a short region of increasing dose would yield mutations with an efficiency significantly exceeding that of the long linear portion of the dosage curve. For physical reasons this is very improbable. If any considerable portion of the spontaneous mutation is, for a particular species, induced by the background radiation, the entire curve, including the origin, would be shifted correspondingly to the right if the natural radiation were included with the applied radiation in the definition of dose. If the background radiation is not included in the dose, the curve and its origin would be unaltered.

Indirect Action

The direct proportionality of mutation frequency to dose does not mean, however, that the high-energy quantum must score a direct "hit" on the deoxyribose nucleic acid of the chromosomes to bring about a mutation. Indirect action is not excluded, provided that the genetic effect is proportional to the ionization produced by the radiation. The effectiveness of chemical mutagens in producing mutations and the alteration of the efficiency of x-rays in producing mutations by modification of the oxygen concentration in the tissues demonstrate sufficiently that indirect, chemical steps may intervene—perhaps always intervene—between the ionization and the mutation. For example, in an atmosphere of oxygen, a dose of 2000 roentgens produces more mutations than it does in an atmosphere of air; and when it is delivered in nitrogen or helium, the frequency of mutations is diminished.

Moreover, a recent study by A. M. Clark of Australia (*8*) demonstrates an effect of the intensity at which the radiation is delivered if the x-rayed spermatozoa are simultaneously subjected to the action of sodium azide. Almost twice as many sex-linked recessive lethal mutations were produced at an intensity of 2000 roentgens per minute as at 100 roentgens per minute. This is taken to mean that chemical mutagens produced by the radiation, and sensitive to the action of azide, can accumulate to higher concentrations when the dose rate is very high, and consequently stand a better chance of producing mutations after diffusing to other points within the nucleus.

This type of finding raises once again the problematical existence of a threshold below which the intensity of the radiation—and consequently the concentration of chemical agents produced by it—is too low to bring about mutations. Under certain conditions, this may ulti-

mately turn out to be the case. However, it should be stressed that under ordinary conditions and with low to moderate dose rates, the linear proportionality and the nonexistence of a threshold appear to obtain. Until we are assured to the contrary, the only safe working assumption is that every dose, even the lowest, is effective in producing mutations and is consequently genetically damaging.

Somatic Cells

It would be a grave mistake to think that mutations of the hereditary material are confined to the reproductive cells, or germ line. They can presumably occur also in the somatic cells of any tissue. At the present time, however, we have all too little knowledge of what happens to mutant somatic cells. Sometimes these cells exhibit a mutant phenotype, and a mosaic individual results. More significant would be dominant or partially dominant effects on essential metabolic and biochemical processes, which might consequently be impaired.

Recent studies by E. B. Lewis of the origin of leukemia (*9*) and by G. Failla of the phenomenon of aging (*10*) suggest that because both of these, like radiation-induced mutations, seem to increase linearly with the dose of ionizing radiation and without sign of a threshold, they too may result from the induction of mutations by radiation and their accumulation in somatic cells. Possibly cancer, in general, may arise through the same cumulative effect, which does not at all exclude the intervention of other types of agents (viruses, nutritive factors, and chemical agents) in the final outburst of malignant growth.

Thus, in some of my own experimental studies with certain strains of *Drosophila*, the induction of two distinct forms of abnormal growth may be initiated either by ionizing radiation or by excessive amounts of tryptophan in the diet (*11*). The genetic basis of the effect comprises, in each case, a mutant gene responsible for the abnormal growth and a suppressor gene that under ordinary circumstances inhibits it. By a moderate dose of radiation (1000 roentgens)—moderate for *Drosophila*—or by alteration of the diet, the effectiveness of the suppressor is destroyed—in this instance by interference with its action, and not by mutation. Thus, radiation or dietary factors may so upset a balanced genetic system as to evoke abnormal forms of growth.

Similarly, radiation might evoke leukemia, or in the case of an accumulation of mutations in somatic cells over a lifetime, might alter the metabolic machinery in such a way as to impair its resistance to variations in the external conditions of the environment, and thus trigger a breakdown. Somatic mutation may be involved, but it is not necessary to explain the phenomena.

Mutation as a Random Process

Geneticists have often been quoted as saying that "mutation is a random process," and this has been much misunderstood. It does not mean, of course, that any imaginable sort of effect can be produced by gene mutation within a particular species. The viable modifications are definitely conditioned by the nature of the genes that mutate and by the harmony of the normal processes of metabolism and development. For example, although eye-color mutations in the fruit fly are numerous and of a considerable variety of colors, and although other species of flies have blue or green eyes, yet it seems to be quite beyond the range of possibility for *Drosophila melanogaster* to acquire, by mutation, a blue or green eye color. The spectrum of change is definitely limited. Nor, in the second place, does the randomness of mutation imply that all genes mutate at the same frequency, either spontaneously or when acted upon by ionizing radiations.

Different genes have different stabilities, and under the same conditions some may mutate 100 times as frequently as others. What the "randomness" is intended to imply is that at the present time there is no way of affecting certain genes and not others, at least by means of radiation. All are equally exposed and mutate with a probability in accordance with their individual stability. Two identical genes, one with a recent history of mutation and the other without, will both possess the same mutability. So far, it is impossible to direct the mutation process. Radiation acts blindly, and that is why the deleterious nature of the vast majority of mutations is so important.

By means of several hundred roentgens of radiation, it might indeed be possible to increase the probability of obtaining a desirable mutation in a spermatozoon or egg cell to a chance of one per thousand. At the same time, the probability of getting a lethal mutation would have risen to one in four, and the probability of getting a mutation with some degree of harmfulness would have risen to virtual certainty. That is why we must wait for the slow processes of evolution to sort out the advantageous changes.

Irreversibility and Deleterious Effect of Mutations

Considering the nature of the alterations brought about by radiation in the hereditary material, and, furthermore, the capacity of the latter to replicate itself exactly, we can readily see why the effects of mutation are essentially irreversible. The loss of a part of the genetic material is irreparable, and a large portion of all the hereditary changes induced by radiation consists of such losses. Alterations in the arrangement of the genetic material can be reversed only by an exact rearrangement to the original conditions, which the laws of probability must make exceedingly rare if the chromosomes are broken more or less at random.

Thus, it is not surprising to find that, although spontaneous mutations may undergo reversion to the original state, the radiation-induced ones have rarely, if ever, been observed to do so. Consequently, once a mutation has been produced by radiation and transmitted to the population, it continues its way from generation to generation unless it is either eliminated by the death or failure of its possessor to reproduce, or is excluded by chance from representation in the progeny.

It is also easy to comprehend why the vast majority of mutations have deleterious effects on their possessors. It is now recognized that many, if not all, genes are concerned with the presence and specificity of particular enzymes, each of which governs some one chemical step in the metabolic pattern. There are extremely few biochemical steps in metabolism that can be altered with impunity, and most of them are in fact essential. It is little wonder, therefore, that when a mutation impairs the specificity of an enzyme it blocks a particular metabolic step more or less completely, and the usual outcome is fatal unless the organism has some alternative way of supplying its needs.

These theoretical considerations, which imply that most mutations are expected to be lethal or at least quite detrimental in nature, are supported by the experimental facts. Thus, in *Drosophila* about one-fourth of all mutations are lethal or semilethal, 15 to 20 percent produce sterility in one or both sexes, and nearly all the remainder, whether producing visible morphological changes or not, are subvital (*12*). Less than one in 100 of all mutations—probably nearer one in 1000—is definitely advantageous under existing conditions, although some of the subvital ones might become neutral or even advantageous under altered circumstances.

Most dominant mutations thus quickly lose out in competition with their previously selected, well-adapted alleles which are already established in the species. Only because most mutations are recessive—which is another way of saying that most genes are fairly efficient in a single dose, so that the alteration or

even loss of a single one of the two alleles representing each kind of gene does not block the controlled reaction—is it possible for harmful mutations to accumulate in the gene pool of a population. However, while recessive, harmful mutations do not produce their maximum damage except when inherited in a double dose, through the mating of heterozygous carriers, nonetheless, as studies both of fruit flies and of mice now make clear, the efficiency of the single normal gene is rarely fully equal to that of two. In other words, there is some slight damage from harmful mutations even when they are heterozygous, some loss of fertility, or some impairment of vitality and shortening of the life span, even though no obvious visible defects are to be seen.

This damage, very difficult to measure quantitatively, nevertheless must bear some relation to the load of hidden mutations, which has recently been estimated by Morton, Crow, and Muller (*13*) as amounting to four lethal equivalents per person in the human species. Against the heterozygous damage of harmful genes must be weighed the possibility that mankind, like the fruit fly, is most vigorous in a heterozygous condition—that optimum vigor may result from the balancing of one set of genes that would be harmful if homozygous against another set that would also be harmful if homozygous.

At this point we must confess our present ignorance and await the results of further experiments. Meanwhile, it must be stressed that whereas the just-mentioned benefit of a hybrid nature may apply to man, it is very unlikely that it applies fully all down the viability spectrum, to include the numerous recessive lethal genes as well as the moderately detrimental mutations. Hence it remains imperative to see that the burden of lethals (and seriously crippling defects) in the population does not become too great. It may not matter too much to an individual if he has some new, favorable genes, if at the same time he is hopelessly afflicted. The principle is the familiar one of the acute ailment: one may be in fine shape in every other respect, but a severe toothache or peptic ulcer or migraine sours one's entire outlook on life.

Background Radiation

We come now to appraise the current exposure of the general population to nuclear radiations. According to the views of most geneticists, although not of all, the effects of that exposure can best be weighed in relation to the magnitude of the spontaneous mutation rate, which is currently responsible for a certain amount of tangible genetic defect in the population and for a certain load of wholly or partially hidden mutations carried in individuals who are heterozygous for them. If one could confidently assume that all spontaneous mutation was attributable to the background radiation of the environment, the problem would be fairly simple. Unfortunately, this cannot be done, since the spontaneous mutation rate is in most organisms demonstrably higher than could possibly be caused by the background.

Many years ago Muller and Mott-Smith (*14*) pointed out that for *Drosophila* not more than about 1/1000 of the spontaneous mutation could be caused by the background radiation. For longer-lived animals, a greater fraction may well be caused by the background, since the over-all mutation rate in different species holds fairly constant (within about one order of magnitude), although the exposure to background radiation increases enormously with length of life. If the low-level radiation of the background in fact causes a proportionate amount of mutation, then in a species that lives a thousand times as long as *Drosophila* and whose gonads are equally exposed, all spontaneous mutation would be caused by the background. Haldane (*15*) has argued that this might possibly hold true for man. Man lives about 365 times as long as *Drosophila,* for their reproductive lifetimes are of the order of 30 days and 30 years, respectively. Thus, while it may not be very likely that for man the "doubling dose" of radiation—that is, the dose that would double the total spontaneous mutation frequency—is as small as the amount of the background radiation, it is quite possible that it may be no greater than three times the background.

In the most recent estimate made by the consultants of the National Academy of Sciences Committee on the Genetic Effects of Atomic Radiation, John S. Laughlin and Ira Pullman (*16*), the previous estimate of the background radiation as amounting to a 4.3-roentgen gonadal dose over a 30-year period has been revised downward to 3.1 ± 0.6 rem. Of this amount, cosmic radiation contributes 0.78 ± 0.09 rem; earth and housing 1.59 ± 0.6 rem; atmospheric radioactivity 0.06 ± 0.03 rem; and internal radioactivity (from K^{40}, C^{14}, and radium), beta and gamma, 0.54 ± 0.09 rem, and alpha, 0.15 ± 0.09 rem.

The internal radioactivity of the body is derived mainly from the beta radiation of potassium-40. The data on terrestrial radiation are still meager, but it is evident that there is considerable variation in its amount, depending on whether a person is over sedimentary rock or soil rather than over igneous rock, and on whether the habitation is wooden rather than brick, stone, or concrete. There are also certain areas where a population living on highly radioactive sands is exposed to considerably greater than the usual amounts of radiation—for example, in Brazil and India. On the coast of Travancore, where a fishing population leads a rather primitive life on monazite sands, the 30-year gonadal dose may possibly be as high as 50 or even 150 roentgens (*17*).

If the doubling dose were equal in size to the background radiation, one would expect the frequency of tangible genetic defects in populations living at a particular background level for a sufficient number of generations to approach an equilibrium at a frequency that would vary directly with the amount of the background radiation. If the threefold difference in frequency of congenital defects observed in certain populations compared with others were caused by a threefold difference in the amount of background radiation, it would follow that the doubling dose was equal in magnitude to the background radiation—that is, 3 roentgens. However, it may be argued against this possibility that if the doubling dose were indeed so low, then the frequency of genetic defect in the Travancore population living on highly radioactive soil should approach a frequency of not less than 30 to 40 percent, a level which might have been noticed even though no close study of the situation has yet been made.

Clearly, this is one question for which a genetic analysis is of extreme urgency. If the average gonadal dose of 10 roentgens per person recommended for the general population as a "permissible limit" by the National Academy of Sciences Committee is in fact 3 times the doubling dose, instead of being, as was thought a year ago, probably not above one-fourth of the doubling dose, then a complete reevaluation of the recommendation is called for.

Fallout

No recent revision with regard to the exposure of the general population to fallout from weapons testing has been made, and the figures of a year ago seem to be accurate enough for an evaluation. The extrapolated gonadal dose of 0.1 roentgen per reproductive lifetime at the average rate of fallout over the past 5 years, or of 0.2 roentgen at the maximum rate, amounts to no more than 1 or 2 percent of the recommended maximum allowance and need not cause undue concern. The localization of iodine-131 in the thyroid and of strontium-90 in bone may arouse concern regarding their somatic effects, such as the induction of leukemia, carcinoma, or shortening of

life, but by the same token their localization lessens gonadal exposures from those sources. On the other hand, there is less evidence that cesium-137, another fallout product of importance and long life, is localized within the body and it might even be concentrated to some measure in the reproductive organs. This possibility must be carefully investigated.

Artificial Sources of Radiation

A year ago, in the Report of the National Academy of Sciences Genetics Committee (*18*), the average gonadal exposure of the United States population to medical and dental uses of x-rays, radium, and radioactive isotopes was given a preliminary estimate, based on the studies of our consultants, J. S. Laughlin and I. Pullman, of about 3 roentgens per reproductive lifetime. Their fuller survey of the available data (*19*) revises the probable dose to the gonads upward to 4.6 ± 3 roentgens. Table 1 presents their estimate broken down into categories of dosage.

They have made it clear (as likewise various radiologists have pointed out) that many of the data on which the estimates are based are limited to particular institutions or situations, that there is very great variation in actual practice, and that the statistical uncertainty of the estimates is great. Nevertheless, no better estimates can be made at this time from available data, and they are in agreement with very similar estimates of the exposure of the Swedish population to diagnostic x-rays which are referred to in statements made by the United Nations Scientific Committee on the Effects of Atomic Radiation (*20*). The British estimate of gonadal exposures to diagnostic x-rays is considerably smaller, largely because the average number of examinations per year per person is lower.

In spite of the higher individual exposures of medical personnel and atomic energy employees, occupational exposures add little to the average gonadal exposure of the whole population because of the relatively small number of such persons. It has been estimated, for the United States and Great Britain, respectively, at 3 to 6 percent of the total exposure due to artificial sources. For such individuals and any others subjected to high individual doses, for whatever reason, the problem becomes one of the dosage level at which there will be a significant increase in the probability of tangible genetic damage to their own children and grandchildren. This is why the National Academy of Sciences Genetics Committee has recommended an upper limit of exposure for occupational risk totaling a 50-roentgen gonadal dose from age 20 to age 30 and another 50 roentgens during the succeeding decade of life. The British committee (*21*) made an almost identical recommendation, though in the form of a lifetime total of 200 roentgens and a limit of 50 roentgens from conception to age 30.

Our uncertainty about the precise levels of current exposure to artificial sources of radiation, and the foregoing rough estimates which indicate that the level may well be approaching 50 per cent of the total recommended "permissible dose" for the general population, make it imperative to set up some sort of personal recording of exposures, difficult though that may be from every practical point of view. It is urgently advisable (i) because we so seriously need more precise data about exposures, and record-keeping is one obvious means to this end, even though it may be supplemented and checked by other methods of recording total doses to the population; and (ii) because the existence of such a system of personal records will probably, more than any other factor, provide the atmosphere of caution and prudence so necessary on the part of both the practitioner and the public. In the year since the Genetics Committee's recommendation was made, no definite steps have been taken by public authorities in this direction, so far as I know. Action, at least in the form of pilot efforts, should be specifically urged upon state and federal health authorities at this time.

Competent radiologists have assured members of the Genetics Committee that it should be possible to reduce the average exposure of our United States population by at least half, without diminishing the needed medical and dental diagnostic information. This will be possible not only through the development of new devices, such as faster films and the amplification of fluoroscopic images, so as to provide the same or better information for less exposure, but also by means of more critical attention to proper shielding, filtration, and definition of beam, by reducing the use of fluoroscopy and certain types of pelvimetry which produce heavy exposures (in the latter case of two individuals in the population at once), and by limiting the use of diagnostic x-rays to situations where the information they provide is truly of value. With prudence and the aid of new developments in radiology which are just around the corner, it may even be possible to reduce diagnostic exposures to one-tenth of the current level, at which point they would become a minor problem.

Table 1. Summary of the gentically effective average gonad doses from medical diagnostic x-ray examinations and radiation therapy treatments received per person during one generation (30 years) by the population of the United States (*19*). The minimum average doses have been computed on the basis of the lowest gonadal doses reported. Even further reduction can be obtained since improved techniques are used for some procedures for which the gonad doses are not yet measured. The probable average doses are based on an average of those reported measurements of techniques generally employed.

	Minimum gonad dose (roentgens)	Probable gonad dose (roentgens)
X-ray diagnostic examinations		
Radiography	1.0	1.8
Fluoroscopy	0.3	1.5
Photofluorograms and mass chest x-rays	0.006	0.006
Dental x-rays	0.03	0.1
Obstetrical x-rays	0.16	0.7
Total diagnostic dose	1.5 ± 1*	4.1 ± 3*
X-ray and radioisotope therapy treatments	0.5	0.5
Total gonad dose	2.0	4.6

* Rough limits of error are added in this table on the basis of a verbal communication from J. S. Laughlin and I. Pullman to the Genetics Committee of the National Academy of Sciences. The "total diagnostic dose" is considered by them to be a much firmer estimate than the figure for therapy treatments and, consequently, than the "total gonad dose."

Peaceful Application of Atomic Energy

Finally, it is necessary to look at the situation which is perhaps most likely to create future hazards in this area—namely, the development of atomic energy for peaceful applications. It is stated on good authority that a 100-megawatt heat reactor will produce annually the same quantity of long-lived fission products as the detonation of a 1-megaton fission bomb (*22*). When it is envisioned that by 1965 Great Britain expects to be producing 6000 megawatts of atomic energy, and that within 20 years the United States may produce 20,000 to 40,000 megawatts, it is quite clear that the problem of the safe disposal of these fission products will become one of major proportions.

True, the fission products will normally be contained; but that does not avoid the problem of ultimate disposal. Can we depend on storage underground, with possible contamination of soil and water supplies? The Los Alamos laboratory alone has already used up 40 acres in underground storage and needs a new

site for that purpose. Or can we envision storage in the ocean depths, with the possibility of an overturn of even stable waters sufficient to contaminate marine plant and animal life, and thus eventually all that of the lands adjoining the sea? The very bulk of these long-lived fission products will be so enormous that containment within corrosion-proof vessels, even for 30 to 50 years, will be virtually impossible.

Moreover, the occurrence of accidents, such as an occasional explosion of a reactor or the wreckage in transit of vehicles carrying radioactive materials, cannot be dismissed as too improbable. Atomic power developed on a large scale cannot be immune to accident, any more than any other kind of human enterprise. If even 1 percent of the long-lived fission products produced at a 20,000 megawatt annual level of atomic power were to be released by leakage and accident, the effect would be equivalent to the radiation from 100 bombs of the Hiroshima size.

The threat to mankind of exposure to radiation arising from the peaceful development of atomic energy may thus far outstrip not only that from current exposures due to weapons testing and fallout but even that from the exposures necessary for medical and dental diagnosis. The only immediately obvious escape from so dire an outcome may lie in the rapid development of the hydrogen fusion process as a source of energy.

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W. Bothe, Experimental Nuclear Physicist

Most of today's nuclear physicists are too young to have known the time in which the foundation of their science was laid. The death of Walter Bothe (8 January 1891–8 February 1957) reminds us of the years in which a handful of gifted researchers made one basic discovery after another with very primitive experimental facilities. Their method of working can no longer be imitated today. The field has become too large, the experimental techniques are too involved. However, their way of thinking, the method they employed in choosing, from many possible problems, the important ones, and the way in which they focused their attention on the physical result in spite of great emphasis on experimental technique can be a lesson for us, particularly today when the extension of the experimental method and its problems can all too easily veil the real goal of physical understanding.

Bothe was a student of Max Planck. He therefore started his career as a theoretical physicist. For his Ph.D. thesis he developed the theory of optical refraction and reflection from the scattering of light by single molecules. Max Planck stressed independence in the work of his students. Bothe liked to tell that Planck only twice made a comment on the calculations that were submitted to him. In the first, he said, "This is still insufficient"; in the second, "Now you may finish."

In 1920, after an interruption of nearly 6 years, caused by World War I and long imprisonment in Siberia, Bothe started, with Geiger, his experimental career in physics at the Physikalisch-Technische Bundesanstalt (the German Bureau of Standards). Even from routine measurements in the laboratory he was able to gain new insight which led to publications. However, he soon turned, fully supported by Geiger, to the fascinating problems which the rapidly developing quantum theory set for experimentalists. Geiger's work with alpha rays was carried on in Rutherford's laboratory. Bothe turned his attention to the behavior of beta rays. With the cloud chamber he examined their tracks and, by means of theory, was able to classify the complicated phenomena. His articles on beta rays in the well-known *Handbuch der Physik* are classic examples of the way in which a confused picture may be clarified by theoretical treatment and appear, finally, quite simple.

That was one of the great periods of physics, marked by the penetration of the concept of quanta into "classical" considerations. A large circle of famous physicists was gathered in Berlin, of whom I shall name only Planck, Einstein, v. Laue, and Nernst. The extensive exchange of ideas between them found visible expression in their joint seminars. There, innumerable problems which arose from the new point of view were discussed. Bothe's entrance into this circle resulted in stimulation for experimental investigations, which he then also performed. The best-known result of these endeavors is his work with Geiger, in which it was shown that, in the scattering of light quanta on electrons (Compton-effect), the law of conservation of energy is valid not only on the average but also for the single elemen-