degree of certainty that the 1:1 ratio of functional sperm carrying the two different homologues, demanded by the usual views of spermatogenesis and the gamete behavior of *Drosophila*, is not being obtained in these experiments, and some other explanation is necessary.

Summary.—Results from the study of segregation of the components of a translocation in the male of *Drosophila* cannot be interpreted easily on the basis of our present assumptions about the nature of spermatogenesis and gamete behavior. It is suggested that in these cases, and in others cited, not all products of spermatogenesis are functional and, further, that this condition may not be limited to these special cases but may be generally true, being revealed only when certain experimental conditions are achieved.

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*SHORTENING OF LIFE IN THE OFFSPRING OF MALE MICE EXPOSED TO NEUTRON RADIATION FROM AN ATOMIC BOMB**

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Introduction.—Only in recent years has evidence begun to accumulate that there are slight dominant deleterious effects of mutations formerly regarded as recessive.[1–4] The results to be reported here, and our earlier work on mice,[3, 5, 6] indicate that such effects may add up to an important part, perhaps the most important part, of the genetic hazards of radiation in man. The evidence from the earlier work on mice is that appreciable deleterious effects of radiation become manifest in the first-generation offspring. This evidence is of two kinds. First, work on radiation-induced mutations at specific loci in spermatogonia has shown

that among the recessive lethals, which comprise more than one-half of all the mutations recovered, many have dominant deleterious effects which, even for individual mutations, are sometimes large enough to be detected easily. Second, over-all population damage was found in the large numbers of animals that are raised as far as three weeks of age in the specific loci studies. In all such experiments carried out, the survival to three weeks of age is significantly lower in the offspring of irradiated males than it is in the controls. (It should perhaps be pointed out that neither of the above effects, nor the effect reported in this paper, is the result of what the geneticist usually refers to as "dominant lethals," which are major chromosomal aberrations that cause early death of embryos and which, as has been pointed out elsewhere,[5] are probably not an important hazard.)

Our earlier work that showed a significant effect on survival to three weeks of age in the offspring of irradiated males led us to expect that there would be measurable deleterious effects later in life. The data reported here show that such is indeed the case. These data furnish a third kind of evidence of first-generation damage and perhaps the most striking one. They were obtained as a by-product of another investigation, and they are not as extensive as we should like. However, they are the only data we have on this subject that were collected under the expensive and difficult conditions of a field test of a nuclear detonation. Furthermore, although the sample was small, it was sufficient to yield a statistically significant effect which appears to be large and, therefore, of general importance.

Materials and Methods.—The material used in the present longevity study was the by-product of an investigation of the relative effectiveness of neutrons from a nuclear detonation and from a cyclotron in inducing dominant lethals in the mouse.[7] In order to reduce the gamma component of the radiation to a proportion that would not appreciably interfere with the estimation of neutron effects, the animals were shielded with lead. The exposure chambers available were lead hemispheres of 7-inch wall thickness and 14-inch inside diameter. Young adult hybrid males, obtained by crossing inbred 101 strain females with inbred C3H strain males, were exposed inside the hemispheres placed at various distances from the detonation. Control males were placed in hemispheres two days before the detonation and for a length of time approximately the same as that required for the exposed animals. Further experimental details are described in the report of the earlier work.[7] One day and a half after the detonation, each male was placed with four adult untreated females of the same hybrid strain. At $18^1/_2$ days after irradiation each surviving male was placed with a new group of four females. Most of the females that became pregnant were killed at a late stage of gestation for the dominant-lethal study. However, since the number of pregnancies turned out to be more than adequate for the dominant-lethal experiment, several of the females were allowed to come to term. It was the offspring of some of these females that were saved for the longevity study described here. All these animals came from matings made from 19 to 23 days after irradiation. A few animals died before weaning, and these were not included in the data reported here. At weaning age the sexes were separated and the animals grouped, so far as possible, six to a cage. They were kept in the same grouping throughout their lifespan. They were checked at least twice weekly for deaths. Only one animal died at less than one year of age, indicating that the conditions under which the animals were kept were good.

The total (neutron plus gamma radiation) dose inside each lead hemisphere was measured, as described in the earlier publication,[7] by means of "tissue-equivalent" ion chambers designed for this purpose at short notice.[8] Subsequently, extensive testing and recalibration of these chambers[9] has led to a revision of the original dose estimates. The doses reported in the present publication are the revised estimates. As was reported earlier,[7] attempts to measure the gamma component of the radiation by means of film dosimeters left a large uncertainty as to the size of this factor. Later tests have been made in which both ionization chambers and chemical dosimeters were used to measure the gamma component inside the lead hemispheres when these were exposed to fission neutrons. According to the latest information,[10] these tests indicate that the gamma-radiation exposure in our experiment was almost certainly less than 10 per cent of the total dose.

Results.—The median and mean lengths of life, together with the number of animals, for each dose group are given in Table 1. An analysis of variance showed that neither grouping in cages nor sex had a significant effect on length of life. It seems likely that larger samples would show some effect of both of these factors, but as there was no significant effect of them in the present experiment, the data were pooled.

TABLE 1

LENGTH OF LIFE IN THE OFFSPRING OF MALE MICE EXPOSED TO NEUTRON RADIATION 19–23 DAYS BEFORE MATING
(Deaths before Weaning Age Excluded)

Total Dose to Parent (rep)*	No. of Offspring	Median Length of Life of Offspring (Days)	Mean Length of Life of Offspring (Days)
0	103	823	792
31	50	741	754
71	5	717	699
118	22	739	723
136	8	666	688
186	2	756	756

* Includes some gamma radiation, estimated to be less than 10 per cent of the total dose.

To test whether there was a significant effect of radiation on the length of life of the offspring, the means were fitted to a straight line by the method of weighted least squares. This gives an intercept of 786 days and a slope of -0.609 ± 0.238. Since the residual variance is less than the within-subclass mean square, there is no evidence of nonlinearity over the dose range tested. Even if the true shape of the curve is nonlinear, it will be conservative, in making the test of significance, to assume linearity. The larger mean square was used to compute the variance of the slope, and a two-sided t-test shows that the slope differs significantly from zero at the 1 per cent level. If one is willing to accept a one-sided t-test as more appropriate, the significance level is 0.5 per cent. Thus there is strong evidence of shortening of life in the offspring of the exposed males.

Discussion.—It is noteworthy that a significant shortening of life was detected in spite of the small sample and the considerable genetic variability that must have been present in a population that was the F_2 of a cross between inbred strains. Furthermore, the weighted mean dose received by the exposed fathers was only moderate, being less than one-sixth of the 30-day median lethal dose as measured from other animals of the same strain exposed under the same conditions at distances

closer to the same detonation. While it is true that certain features of the experiment, which will be discussed later, tended to maximize the shortening of life, nevertheless the result observed appears to be so large that it seems quite possible that shortening of life is an effect that might be detectable in studies of the offspring of exposed parents in human populations.

In view of the lack of information on this subject, and specifically the fact that no data of this nature were ready for consideration prior to the writing of the 1956 report of the National Academy of Sciences Committee on Genetic Effects,[11] it is desirable to consider what the present data might indicate when they are extrapolated to man. Taking the estimate obtained from the curve fitted to the mouse data, and assuming that the shortening of life in man would be proportional to this, gives, on the basis of a 70-year length of life in man, the figures shown in Table 2. It should be kept in mind that the results were obtained from neutron

TABLE 2

SHORTENING OF LIFE IN THE OFFSPRING OF FATHERS EXPOSED TO NEUTRON RADIATION 19–23 DAYS BEFORE MATING

OBSERVED RESULT IN THE MOUSE AND EXTRAPOLATION TO MAN
(Deaths before Weaning Age Excluded)

	Mouse	Man
Point estimate	0.61 day/rep to father	20 days/rep to father
Lower 95 per cent confidence limit	0.14 day/rep to father	5 days/rep to father
Upper 95 per cent confidence limit	1.07 day/rep to father	35 days/rep to father

irradiation. The relative biological effectiveness of neutrons for this effect is not known, but it seems likely, from other data on mutations, that gamma and X-radiation would be less effective than neutrons. It should also be emphasized that the effect observed here is probably a maximum one, since the offspring were obtained from matings made between 19 and 23 days after irradiation. Our data from experiments on mutations at specific loci[12] indicate that the sperm utilized in matings made within this time interval would have been derived from cells in a sensitive stage of gametogenesis at the time of irradiation. From approximately two to four times as many mutations are recovered from this stage as from the spermatogonial stage, which is the important one so far as radiation hazards in man are concerned.[6] It is also possible that the spectrum of mutations from irradiated spermatogonia would be qualitatively different and, conceivably, less effective in shortening life. However, there is no direct evidence of this, whereas there is evidence from our specific loci studies that some mutations induced in spermatogonia have, even individually, a dominant effect on length of life that is detectable. To summarize this paragraph: it should be remembered that the estimates given in Table 2 are based on neutron irradiation of a post-spermatogonial and sensitive stage in gametogenesis and that X- or gamma irradiation of spermatogonia would almost certainly produce a smaller effect.

Another way of considering the magnitude of the observed result, so far as its human implications are concerned, is to compare the shortening of life in the offspring of irradiated fathers with that in the irradiated individuals themselves. The data on shortening of life of the males exposed to this same detonation will be presented in detail elsewhere. Briefly, the percentage shortening of life of these animals, based on 24 controls and 128 exposed animals, is 0.078 per cent per rep.

The present data, expressed in the same form, give 0.077 per cent shortening of life in the offspring for each rep received by the father, that is, approximately as much effect as on the exposed individuals. Thus the best estimate from our present data is that, for neutron irradiation of the sensitive stages in spermatogenesis, the shortening of life in the offspring of irradiated males will be similar in magnitude to that in the exposed individuals. Again, the effect from irradiation of spermatogonial stages would probably be less. Whether the *ratio* of effect in offspring to effect in exposed individuals will be different for X- and gamma rays from that observed for neutrons will, of course, depend on whether the relative biological effectiveness of neutrons is different for the effect on the offspring and the effect on the exposed individuals. Present, incomplete data on these points give no grounds for expecting that the ratio of effect in offspring to effect in exposed individuals will be less for X-rays than for neutrons. Weighing the evidence reported here, and making some allowance for the many uncertainties, it seems reasonable to predict that, even under the conditions of radiation exposure in man, shortening of life in the offspring of irradiated fathers will be between 10 and 100 per cent of the shortening of life in the exposed individuals themselves. It should be remembered that this excludes an additional effect on the offspring, namely, as measured in the mouse, death before weaning age. Also, and more important, since the shortening of life is probably the result of mutations with slight dominant effects, the damage would not end with the first-generation offspring but would, to a certain, and probably large, degree, be transmitted to later generations.

Summary.—Length of life in the offspring of male mice exposed to moderate doses of neutron radiation from a nuclear detonation is shortened by 0.61 day for each rep received by the father over the dose range tested. This figure excludes death before weaning age. The 95 per cent confidence limits are 0.14 and 1.07 days per rep. Extrapolating to a proportional shortening of life in man gives 20 days per rep received by the father as the point estimate and 5 and 35 days as the 95 per cent confidence limits. The offspring were obtained from matings made from 19 to 23 days after irradiation and therefore represent the effect of irradiation on germ cells in a post-spermatogonial and sensitive stage of gametogenesis. It is probable that irradiation of spermatogonia (the stage that is important from the point of view of human hazards) would give a somewhat smaller effect. However, since the present data show an effect on the offspring which is as large as the shortening of life in the exposed individuals themselves, it seems likely that, even when allowance is made for the conditions of human radiation exposure, shortening of life in the immediate descendants will turn out to be of a magnitude that will warrant serious consideration as a genetic hazard in man.

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CORRELATED SELECTION FOR MOTILITY AND SEX-INCOMPATIBILITY IN ESCHERICHIA COLI K12

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Sexual fertility in *Escherichia coli* is influenced by a number of factors, environmental and genetic.[1] One of the latter is F, which is diagnosed by the following rules of compatibility: $F^+ \times F^+$ and $F^+ \times F^-$ are fertile, but $F^- \times F^-$ is sterile. The wild-type K12 strain is F^+, but "self-incompatible" F^- mutants have appeared sporadically in laboratory cultures. Among the genetic elements of *E. coli*, F is remarkable for its high contagiousness: F^- cells become F^+ when the two types are grown in mixed culture. Furthermore, the progeny of $F^+ \times F^-$ crosses are uniformly F^+. Therefore, a reliable method of obtaining F^- derivatives of various stocks would be desirable as a technical help[2] as well as for its possible clarification of the nature of F.

In the course of immunogenetic studies of *E. coli*, various strains were *motilized*, that is, passed through semisolid agar to select for the highest motility and development of flagellar antigens. Many of the selected clones proved to be F^-. The experiments reported here indicate that this is a result of a selective advantage of F^- mutants rather than a direct induction of them by the technique.

Experimental.—The motilization medium (NGA) consists of nutrient broth plus 8 per cent gelatin and 0.4 per cent agar.[3] Comparable results were obtained in the same medium without gelatin. In these media, nonmotile bacteria grow only at the site of inoculation, while motile bacteria eventually swarm through the medium. After an initial lag, swarms appear from which faster swarms may arise in turn. The fastest rate of swarming observed on this medium (at 37° C.) was 3 mm/hr. The succession of faster swarms upon subcultures on fresh NGA medium,