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# Radiation and the Sex Ratio in Man

## Sex ratio among children of survivors of atomic bombings suggests induced sex-linked lethal mutations.

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In species with an XX-XY type of chromosomal sex determination, such as man, the distribution to the offspring of radiation-induced, sex-linked mutations will differ according to the sex of the radiated parent. Furthermore, in the human species the nonhomologous nature of the X- and Y-chromosomes, coupled with the genetic inertness of the Y, permits the more frequent manifestation of sex-linked recessive genes in the heterogametic sex—namely, the male. This difference in manifestation and distribution of sex-linked genes would lead us to expect a significant change in the sex ratio if human populations were sufficiently exposed to mutagenic factors such as x-rays, or the fallout from weapon testing. Specifically, if fathers alone were exposed, an increase in the frequency of male births would be expected because sex-linked lethal mutants induced by the exposure would be transmitted only to the exposed fathers' daughters. If mothers alone were exposed, a decrease in the frequency of male births would be expected because sex-linked recessive mutants would more frequently find expression in the sons rather than in the daughters of the exposed females. If both parents were exposed, and if the effects of parental exposure were additive although not necessarily equal, we would expect a decrease in the frequency of male births; the change, however, would not be expected to be as pronounced as when mothers alone were exposed.

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### Assumptions

Several assumptions are implicit in postulating the changes just mentioned, and it seems important to state explicitly, at the outset, these assumptions, with a brief justification for each. Firstly, it is assumed that although autosomal lethal or semilethal mutations which are sex-limited may occur, their net effect is not such as to obscure the different effects on the sex ratio of paternal versus maternal radiation. Clearly, were this not so, the deviations postulated could be altered in degree or direction depending upon the relative frequencies of male-limited or female-limited mutants, or both. In view of the current state of knowledge of radiation genetics, it seems appropriate to assume that the predominant change in the sex ratio will stem from sex-linked rather than sex-limited effects.

Secondly, it has been assumed that the effect on the sex ratio of genes in the Y-chromosome is negligible, and that there exist no homologous portions of the X- and Y-chromosomes. The reasonableness of the former is supported by the knowledge that there is known, at present, no single, well-documented case of holandric inheritance, although this form of genetic transmission should be easy to recognize [for a discussion of Y-borne inheritance, see Stern (*1*)]. The legitimacy of the assumption that there is no homology between the X- and Y-chromosomes rests on the cytological work of Mathey (*2*) and Sachs (*3*).

Thirdly, and with reference to the exposure of both parents, it is assumed that sex-linked recessive mutants would outnumber sex-linked dominant mutations. The only animal for which data exist relevant to this assumption is *Drosophila melanogaster,* and here sex-linked recessives are estimated to be several times more common than sex-linked dominant mutants. In this connection, however, attention must be called to the

Table 1. Summary of the findings of Kaplan (*7*) and of Macht and Lawrence (*6*) with regard to the frequency of male births following parental exposure to ionizing radiations.

| Exposed parent | Estimated dose (r) | Total offspring of known sex born after radiation | Male | Female | *p* |
|---|---|---|---|---|---|
| | | *Kaplan, 1956* | | | |
| Mother | 50–200 | 407 | 200 | 207 | 0.4914 |
| | | *Macht and Lawrence, 1955* | | | |
| Father | Unknown | 4277 | 2198 | 2079 | 0.5139 |
| None | Control | 3491 | 1830 | 1661 | 0.5242 |

evidence which suggests that sex-linked spontaneous mutation occurs more frequently in the human male than in the female (*4, 5*). The possibility must be entertained that the same may hold true for sex-linked induced mutations. If this is, in fact, true, then maternal exposure may not lead to a relatively greater effect on the sex ratio than paternal exposure. The directions of deviation of the sex ratio would not of course be altered even if induced sex-linked mutations occurred more frequently in the male than in the female. One other assumption which has been made in the analysis of the data presented below is that the increase in gene mutations with increasing radiation is linear over the measurable range of exposures. The linearity of the response in gene mutations to dose of radiation is one of the cornerstones of radiation genetics, and rests on a literature far too extensive to review here. Suffice it to say that since linearity obtains in all organisms thus far studied, it seems improbable that a different situation would obtain in man.

## Studies of the Sex Ratio

To date, four studies on man have reported information on the sex ratio among infants born subsequent to parental exposure to ionizing radiations. These are the observations of Macht and Lawrence (*6*) on the offspring of American radiologists; of Kaplan (*7*) on the pregnancies occurring to women following the use of x-ray therapy to correct an apparent sterility; of Turpin, Lejeune, and Rethore (*8*) on the sex of children born to French men and women receiving x-ray therapy for sciatic neuralgia and a variety of other complaints; and, lastly, of Neel and Schull (*9*) on pregnancy terminations to survivors of the atomic bombings of Hiroshima and Nagasaki. We present in Table 1 a summary of the findings of Kaplan and of Macht and Lawrence; in Table 2, the findings of Turpin, Lejeune, and Rethore; and in Tables 3 and 4, the findings of Neel and Schull. In the presentation of these data, we give, when it has been published, the author's estimate of the average exposure (or the range) sustained by the various groups of individuals. Let us be the first to recognize the tenuous nature of these estimates; however, since we shall be principally concerned with the direction of deviation of the sex ratio rather than the magnitude of the change, precise specification of the dose is less important, in a sense, than the proper ranking of the various exposure groups.

In a discussion of the data presented in Tables 1 to 4, one can deal rather briefly with the findings of Kaplan and of Macht and Lawrence (Table 1). In Kaplan's case, there does not exist a satisfactory unexposed control for his observations, nor have the data been presented in a fashion such that the proportion of male births could be regressed on different maternal exposures (generally Kaplan's cases received 200 roentgens, but some appear to have received less). In Macht and Lawrence's data, it is impossible to estimate the average exposure of radiologists in the United States as contrasted with physicians who are not radiologists. It is worth noting, however, that the direction of deviation in Kaplan's data would appear to be in keeping with genetic theory, for the frequency of male births is less than in the general population; this may not, however, be a meaningful comparison. The direction of deviation in Macht and Lawrence's data, on the other hand, is contrary to genetic theory; there are proportionately fewer, rather than more, males when the fathers were exposed.

Turpin, Lejeune, and Rethore's observations (Table 2) warrant somewhat more extended discussion. These authors selected for study, from the radiotherapy

Table 2. Summary of the findings of Turpin, Lejeune, and Rethore (*8*) with regard to the frequency of male births following parental exposure to ionizing radiations.

| Exposed parent* | Estimated dose (r) | Reproductive performance before exposure | | | | | Reproductive performance after exposure | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Total matings | Total children of known sex | Male | Female | *p* | Total matings | Total children of known sex | Male | Female | *p* |
| | | | | | *All cases* | | | | | | |
| Father (b) | Unknown | 66 | 112 | 62 | 50 | 0.5536 | 52 | 96 | 42 | 54 | 0.4375 |
| Father ($C_1$) | 1295 | 284 | 465 | 242 | 223 | 0.5204 | 194 | 275 | 157 | 118 | 0.5709 |
| Father ($C_2$) | 1461 | 137 | 231 | 116 | 115 | 0.5022 | 95 | 130 | 68 | 62 | 0.5231 |
| Mother | 1360 | 154 | 236 | 130 | 106 | 0.5508 | 97 | 136 | 63 | 73 | 0.4632 |
| | | | | | *Only cases having children before and after exposure* | | | | | | |
| Father ($C_1$) | 1295 | 92 | 150 | 79 | 71 | 0.5267 | 92 | 119 | 66 | 53 | 0.5546 |
| Father ($C_2$) | 1461 | 42 | 67 | 30 | 37 | 0.4478 | 42 | 51 | 27 | 24 | 0.5294 |
| Mother | 1360 | 45 | 61 | 37 | 24 | 0.6066 | 45 | 51 | 26 | 25 | 0.5098 |

* An explanation of the subdivisions of paternal exposure will be found in the text.

files of all the hospitals in and around Paris, 4428 individuals who had received radiotherapy between 1925 and 1952, a substantial majority having been treated between 1940 and 1952, and where the estimated skin dose was in excess of 300 roentgens. Two other restrictions were placed upon the cases to be selected—namely, the radiotherapy had to be for complaints of a noncancerous nature, and the exposed persons were to be adults less than 35 years of age, if female, and less than 40, if male. Repeated questionnaires were then sent to these individuals. In all, questionnaires were sent to 3579 males, of whom 37.4 percent (1334) responded, and 849 females, of whom 33.5 percent (284) responded. Turpin *et al.* do not present data which would afford some indication of how representative the respondents were of the whole group queried. This is, of course, a problem of real concern in all questionnaire surveys, and especially in those surveys where only a minority of those queried bother to respond.

Be this as it may, the irradiated males were divided by these authors into three groups (a) 368 cases where the x-ray was delivered high up on the lumbar region, or to the thigh, (b) 180 cases where irradiation was to the pelvic area but with the gonads probably shielded, and (c) 786 cases where the subjects were irradiated in the pelvic area under conditions making protection of the gonads impossible. Turpin *et al.* present data on reproductive performance for groups (b) and (c), but not for group (a). In the analysis of their data, group (b) is rejected because of the uncertainty regarding the amount of radiation received by the group. The third group, (c), was further subdivided into individuals treated for "sciatic neuralgia" [517 cases (group $c_1$)], and for various other complaints [269 cases (group $c_2$)].

Turpin *et al.* use, as is apparent from Table 2, the reproductive performance of the exposed individuals prior to their exposure as the base of reference with which to compare reproductive performance after exposure. This procedure leads to a confounding of age and parity effects with those due to radiation. The importance of this confounding is difficult to assess. We know (i) that first-born children are more frequently males than children in subsequent birth ranks (*10*), and (ii) that the frequency of male births tends to decrease with advancing maternal or paternal age (*11*). It is not clear whether the correlation between birth rank and frequency of male births is due wholly or in part to the correlation between birth rank and parental age. Conceivably this confounding could, then, lead to an overestimation of maternal exposure effects and an underestimation of paternal effects.

The extent of this over- or underestimation is in part a matter of speculation; however, Ciocco (*10*) has found that the sex ratio among first born is 0.5153 and that the sex ratio among fifth or higher order births is 0.5124. This change would be the equivalent of approximately 50 rep of maternal exposure, judging from the Japanese data (see below). It is not our purpose to present a critique of the data of Turpin *et al.*, but merely to indicate that this study, like all of the others, including our own, suffers from several deficiencies. One must, therefore, exercise considerable caution

Table 3. Summary of the findings in Japan with regard to the association of the frequency of male births and parental exposure. *Only one parent exposed.*

| Father only exposed | | | | Mother only exposed | | | |
|---|---|---|---|---|---|---|---|
| Total births | Male births | $p$ | Estimated mean exposure (rep) | Total births | Male births | $p$ | Estimated mean exposure (rep) |
| *Neel and Schull, 1956 (1948–1953) (9), parents unrelated* | | | | | | | |
| 31,904 | 16,613 | 0.5207 | 0 | 31,904 | 16,613 | 0.5207 | 0 |
| 3,670 | 1,892 | 0.5155 | 8 | 14,684 | 7,681 | 0.5231 | 8 |
| 839 | 442 | 0.5268 | 75 | 2,932 | 1,474 | 0.5027 | 75 |
| 534 | 284 | 0.5318 | 200 | 1,676 | 850 | 0.5072 | 200 |
| *Neel and Schull, 1956 (1954–1955) (9), parents unrelated* | | | | | | | |
| 11,640 | 6,067 | 0.5212 | 0 | 11,640 | 6,067 | 0.5212 | 0 |
| 1,498 | 774 | 0.5167 | 8 | 4,926 | 2,512 | 0.5099 | 8 |
| 387 | 211 | 0.5452 | 75 | 1,026 | 562 | 0.5478 | 75 |
| 219 | 113 | 0.5160 | 200 | 592 | 311 | 0.5253 | 200 |
| *This article (1948–1953), parents related* | | | | | | | |
| 2,622 | 1,396 | 0.5324 | 0 | 2,622 | 1,396 | 0.5324 | 0 |
| 295 | 152 | 0.5153 | 8 | 963 | 466 | 0.4839 | 8 |
| 83 | 46 | 0.5542 | 100 | 258 | 134 | 0.5194 | 100 |

Table 4. Summary of the findings in Japan with regard to the association of the frequency of male births and parental exposure. *Both parents exposed.*

| Total births | Male births | $p$ | Estimated mean exposure (rep) | |
|---|---|---|---|---|
| | | | Mother | Father |
| *Neel and Schull, 1956 (1948–1953) (9), parents unrelated* | | | | |
| 5994 | 3053 | 0.5093 | 8 | 8 |
| 658 | 337 | 0.5122 | 8 | 75 |
| 422 | 225 | 0.5332 | 8 | 200 |
| 703 | 354 | 0.5036 | 75 | 8 |
| 615 | 319 | 0.5187 | 75 | 75 |
| 192 | 94 | 0.4896 | 75 | 200 |
| 318 | 165 | 0.5189 | 200 | 8 |
| 145 | 72 | 0.4966 | 200 | 75 |
| 145 | 71 | 0.4896 | 200 | 200 |
| *Neel and Schull, 1956 (1954–1955) (9), parents unrelated* | | | | |
| 1474 | 806 | 0.5468 | 8 | 8 |
| 220 | 129 | 0.5864 | 8 | 75 |
| 174 | 101 | 0.5805 | 8 | 200 |
| 212 | 111 | 0.5236 | 75 | 8 |
| 107 | 53 | 0.4953 | 75 | 75 |
| 66 | 35 | 0.5303 | 75 | 200 |
| 89 | 48 | 0.5393 | 200 | 8 |
| 43 | 20 | 0.4651 | 200 | 75 |
| 33 | 18 | 0.5455 | 200 | 200 |
| *This article (1948–1953), parents related* | | | | |
| 394 | 208 | 0.5279 | 8 | 8 |
| 69 | 38 | 0.5507 | 8 | 100 |
| 54 | 29 | 0.5370 | 100 | 8 |
| 43 | 21 | 0.4884 | 100 | 100 |

in any interpretation of the data on the sex ratio. Be this as it may, it is interesting to observe that of the four comparisons afforded by all of the data presented by Turpin *et al.*, three are in the direction which one would expect on genetic grounds.

## Japanese Data

Before we turn to a description of the Japanese data, it is important that one rather important fundamental difference between the study in Japan and those previously mentioned be pointed out. The data of Kaplan, Macht and Lawrence, and Turpin *et al.* involve observations on individuals whose exposure was distributed over some interval in time. Thus Macht and Lawrence's observations are on persons whose total dose may be appreciable, but this dose was incurred at relatively low levels and over a considerable period of time. Kaplan's individuals received three exposures of 50, 75, and 75 roentgens, and the interval intervening between successive exposures was 7 days. Turpin *et al.* do not state that the individuals in their study received repeated exposures; however, if the practice of radiotherapy in France is similar to that in the United States, this is undoubtedly so. The observations from Hiroshima and Nagasaki, on the other hand, are on individuals who received but a single exposure.

In the past, this distinction would perhaps not have been considered important since the data from *Drosophila,* for example, suggest that the critical factor is the total dose and not the period of time over which this dose occurred. Recently, however, Russell (*12*) has presented data on the mouse which suggest that the effect of chronic irradiation for a given dose and in terms of the frequency of the induction of specific locus mutations is less than the effect of acute irradiation. Russell states "Results obtained from an accumulated dose of 600 r given to spermatogonia at approximately 100 r/wk continuous irradiation show a much lower mutation rate than that obtained earlier with a 600 r acute dose of x-rays." The same also appears to be true at a total dose of 100 roentgens. If this finding is confirmed, and if the same phenomenon holds true in man, then there are reasons for believing that the Japanese data are not comparable to the studies in the United States and France.

The Japanese data concerning the effects of radiation on the sex ratio fall into three categories, as follows, two of which (i and ii) have been presented previously (*9*), but analyzed differently, one of which (iii) is presented here for the first time: (i) the sex ratio in infants born to *unrelated* parents in the years 1948–1953, these infants all examined by Japanese physicians; (ii) the sex ratio in infants born to *unrelated* parents in the years 1954–1955, sex reported by the parents but not verified by a physician examiner; (iii) the sex ratio in infants born to *related* parents in the years 1948–1953, these infants all examined by physician examiners. [A description of the background of these children will be found in Schull's report (*13*)].

Detailed presentation of the method of data collection and the bases for the dosage estimates for the parents will not be attempted here, since this material has been described by Neel and Schull (*9*) and Schull (*13*). The present method of analysis was an outgrowth of an effort to integrate the findings on the offspring of related parents with those previously reported on the pregnancy terminations of unrelated parents. In the analysis to follow, we have treated the data as if they were the results from three separate, but similarly oriented, experiences. The decision to do this was based upon two considerations. Firstly, the information collected in the years 1948–1953 involved direct observations by physicians on newly born infants, whereas the information obtained in 1954–1955 was based upon municipal birth records supplemented by a questionnaire to the parents. The two methods of collecting data would seem sufficiently different to justify maintaining a distinction between the two bodies of data which were collected. Secondly, within the years 1948–1953, the division of the data into observations on the offspring of related and unrelated parents seems appropriate in view of the frequently voiced belief that the increased homozygosity of the inbred child may make it a more sensitive indicator of genetic damage, and direct combination of these data was not feasible because of the dissimilarity in the frequency of consanguineous marriages in the various exposure classes. Let us turn now to a brief description of how the data have been analyzed, and a presentation of the results which were obtained.

As we have indicated, we have, in effect, three experiences, and the information with respect to each of these three experiences can be further subdivided into three parts—namely, pregnancies where the mother was exposed but the father was not, where the father was exposed but the mother was not, and where both parents were exposed. Within each of these nine "experience-exposed parent(s)" groups, there exist three or more dosage levels. Thus it is possible to fit nine linear regressions of the frequency of male births on the dose of radiation received by the parent(s). Six of these regressions will be of the form

$$E(p_i) = \bar{p} + b(d_i - \bar{d}),$$

where $E(p_i)$ is the expected proportion of males in the $i^{th}$ exposure class, $\bar{p}$ is the mean proportion of males, $d_i$ is the dose in the $i^{th}$ exposure class, $\bar{d}$ is the average dose, and $b$ is the regression coefficient. Three of the regressions will be of the form

$$E(p_{ij}) = \bar{p} + b_1(F_i - \bar{F}) + b_2(M_j - \bar{M}),$$

where $b_1$ and $b_2$ are now partial regression coefficients, $F_i$ and $M_j$ are, respectively, the doses in the $i^{th}$ paternal and $j^{th}$ maternal exposure groups, $\bar{F}$ and $\bar{M}$ are the mean paternal and maternal exposures, and $\bar{p}$ is, again, the mean proportion of male births. The regressions which were, in fact, fitted were weighted to allow for the differences in the numbers of observations at the various exposure levels. The weights which were used were the reciprocals of the variances (the information) of the proportions of males at the different dosage levels. The final weights were obtained by iteration, starting with the observed proportions as trial values. The intercepts and regression coefficients which were obtained are presented in Table 5. Several comments on these values are in order.

1) It should be noted that no less than 11 of the 12 regression coefficients are of the sign anticipated by genetic theory —that is to say, the deviation is in the direction anticipated if sex-linked mutations have been induced by the exposure. The one nonconforming coefficient is that for mothers unrelated, 1954–1955. The prior probability that 11 or more of 12 regression coefficients will have signs in keeping with genetic theory, if the signs of these regression coefficients are, in fact, equiprobable, is approximately 1 in 341. Clearly the array of signs is significant.

2) Only one of the regression coefficients can be shown to be significantly different from zero, at the 5-percent level of significance, and, unfortunately none of the common regression coefficients for mothers only exposed, fathers only exposed, or both parents exposed differs significantly from zero. It should be mentioned here that substantially the same results are obtained if the arc sin transformation is used.

3) It will be noted from Table 3 that certain observations—namely, those where both parents were unexposed—occur more than once. This, of course, implies that the regression coefficient for "fathers only exposed, 1954–1955," say, is not wholly independent of the regression coefficient for "mothers only exposed, 1954–1955." It may, therefore, be argued that we are not, in fact, dealing with 12 independent regression coefficients since some data are scored twice. This difficulty can be avoided, at the expense of some observations, by omitting entirely the observations on both parents unexposed, and basing the regression coefficients on only those data where the "exposed" parent experienced some irradiation. When this is done, we find that 10 of these 12 estimates have the signs one would expect from genetic theory under these circumstances. A simple sign test reveals that approximately 2 times in 100 we would expect this distribution of signs, or one favoring genetic theory even more if, in fact, the null hypothesis were true.

Table 5. Means and regression coefficients obtained by fitting a weighted linear regression of the proportion of male births to average group exposure in the Japanese data. The values in parentheses are those obtained when unexposed parents are rejected.

| References: Neel and Schull, 1956 (9); Schull and Neel, 1958 (this article) | Father only exposed | | Mother only exposed | | Both parents exposed | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Father | | Mother | |
| | $\bar{p}$ | $b$* | $\bar{p}$ | $b$ | $\bar{p}$ | $b$ | $\bar{p}$ | $b$ |
| 1948–1953 | | | | | | | | |
| Unrelated parents | 0.5202 | 0.0058 (0.0094) | 0.5213 | −0.0101† (−0.0111) | 0.5102 | 0.0039 | 0.5102 | −0.0037 |
| Related parents | 0.5307 | 0.0188 (0.0423) | 0.5204 | −0.0116 (0.0386) | 0.5310 | 0.0024 | 0.5310 | −0.0179 |
| 1954–1955 | | | | | | | | |
| Unrelated parents | 0.5211 | 0.0039 (0.0047) | 0.5186 | 0.0090 (0.0141) | 0.5464 | 0.0137 | 0.5464 | −0.0269 |
| Common regression coefficients | | 0.0056 | | −0.0080 | | 0.0036 | | −0.0042 |

* Regression coefficients are given as increase or decrease in proportion of male births per 100 rep.
† Significant at the 5-percent level.

## Analysis

The findings in the Japanese data pose two very interesting and important questions. (i) How much confidence can we place in these findings as evidence of radiation-induced genetic damage? (ii) If the changes in the sex ratio are, in fact, manifestations of genetic damage, why do we not find evidence for a radiation-induced change in the frequency of congenital malformations or one of the other attributes of a pregnancy termination? In this connection, it should be stated that an analysis of radiation effects in the consanguineous material with respect to malformation frequency and frequency of stillbirths and neonatal deaths, to be presented in detail elsewhere, fails to yield results comparable to those regarding sex ratio, in their negativity confirming the findings reported earlier for the children born to unrelated parents (*9*). Clearly a categorical answer to either of these questions is impossible; however, certain observations seem pertinent to any answer which one may arrive at.

With respect to the first of these two questions, we have indicated elsewhere (*9*) the interpretive difficulties which arise when one begins to select, in the Japanese data, specific cells or groups of cells on which to base comparisons. The present approach would, however, seem to avoid many of these difficulties since (i) all of the data are used, and (ii) the division of the data was based upon a priori considerations regarding parental exposure, relationship, and method of data collection alone, and did not involve value judgments regarding the extent to which one portion of data, collected at one time and in one manner, was *in pari materia* with another collected at the same time and in the same manner.

It must be pointed out, however, that the sex ratio, as a variable, leaves much to be desired, the elegant genetic argument which can be advanced for expecting changes in the sex ratio consequent to parental exposure notwithstanding. Any number of factors—for example, maternal age, paternal age, parity, war, and so forth—seem capable of altering the sex ratio, and though these effects are, in general, small, adequate explanation for the peculiar variations which occur due to these factors has not been advanced. Perhaps the greatest recommendation for accepting the observations with regard to the sex ratio as a manifestation of a real effect of parental exposure is the consistency of the findings. It is true, however, that one does not find within the Japanese data other evidence of sex-linked lethal genes which might logically be expected, such as an increase in the difference in frequency between inviable males and inviable females as maternal exposure increases. The significance of this absence of what might be termed "secondary effects" is not readily appraised since (i) the direct effect on the sex ratio is itself small and (ii) the sex difference in viability has been measured only for the period from approximately the 21st week of gestation onward. Thus, sex-linked lethal mutants leading to gametic death or to the early death of the zygote would not come within our ken.

A further possible recommendation for accepting the results as real is the apparent "reasonableness" of the change. The following rather simple calculation illustrates this: The average number of induced sex-linked lethal mutants at any given dose of radiation is equal to the product of the number of genetic loci at risk, the probability of inducing a mutant per unit dose, and the dose received. If we accept 0.0060 as the best estimate of the change in the sex ratio following 100 rep of maternal irradiation, and if we assume that the number of "targets"—that is, sex-linked lethal producing genetic loci on one X-chromosome—lies between 250 and 2500, then we find that the probability of a sex-linked lethal mutation per rep lies in the interval $2.4 \times 10^{-7}$ and $2.4 \times 10^{-8}$. Current genetic thinking would tend to suggest that the number of loci at risk is rather nearer 250 than 2500, and hence that the sensitivity of human genes would be more likely to be of the order of $2.4 \times 10^{-7}$, a figure which agrees well with the findings for the only other mammal studied thus far, the mouse (*14*), but which suggests a significantly greater sensitivity than that observed in *Drosophila*.

With respect to the second of the two questions raised above, concerning the

implications for the validity of the sex-ratio findings of the failure to demonstrate parallel changes with regard to the frequency of malformations or stillbirths or neonatal deaths, it should be pointed out that Neel (*15*) has recently suggested, on the basis of an analysis of certain aspects of the Japanese data and a comparison of the findings with those available for Caucasian populations, that a significant fraction of congenital malformations may be the segregants from complex homeostatic genetic systems. If this viewpoint is correct, then it follows that induced mutations at loci involved in these homeostatic systems, while ultimately resulting in an increase in malformation frequency, would not be expected to bear the same simple and immediate relationship to malformation frequency as sex-linked lethal mutations do to the sex ratio. It may well be, then, that no conflict of evidence is involved in the failure to demonstrate an effect of radiation exposure on malformation frequency in the first postbomb generation.


## Summary

An analysis of new data concerning the sex of children born to the survivors of the atomic bombings of Hiroshima and Nagasaki, together with a reanalysis of the data previously presented by Neel and Schull (*9*), reveals significant changes in the sex ratio of these children, changes in the direction to be expected if exposure had resulted in the induction of sex-linked lethal mutations (*16*).


### References and Notes


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16. The data here presented were collected under the auspices of the Atomic Bomb Casualty Commission, Field Agency of the National Academy of Sciences–National Research Council of the United States and the National Institute of Health of Japan. Analysis of these data was sponsored by the U.S. Atomic Energy Commission under a grant to the University of Michigan [contract AT(11-1)-405].

# News of Science

## Role of Director of Defense Research and Engineering under the Department of Defense Reorganization Act

One of the elements of the Department of Defense Reorganization Act (now signed into law by President Eisenhower) that has brought forth little criticism from opponents of the bill is that calling for the appointment of a "Director of Defense Research and Engineering." In his message to Congress of 3 April, the President, pointing to the history of interservice rivalries in the research field, the intensification of these conflicts in recent times, particularly in regard to missile development, and the folly implicit in tolerating "this unwise service competition in this critical area," offered the following solution:

### President's Request

"To give the Secretary of Defense the caliber of assistance he requires in the research area, I recommend that the new position of Director of Defense Research and Engineering be established in place of the Assistant Secretary of Defense for Research and Engineering. I believe his salary should be equal to that of the secretaries of the military departments. He should rank immediately after the service secretaries and above the defense assistant secretaries. As the principal assistant to the Secretary of Defense for Research and Development, he should be known nationally as a leader in science and technology. I expect his staff, civilian and military, also to be highly qualified in science and technology. This official will have three principal functions: first, to be the principal adviser to the Secretary of Defense on scientific and technical matters; second, to supervise all research and engineering activities in the Department of Defense, including those of the Advanced Research Projects Agency and of the Office of the Director of Guided Missiles; and, third, to direct research and engineering activities that require centralized management. Further, it will be his responsibility to plan research and development to meet the requirements of our national military objectives instead of the more limited requirements of each of the military services. It is of transcendent importance that each of our principal military objectives has strongly and clearly focussed scientific and technical support.

"With the approval of the Secretary of Defense, this official will eliminate unpromising or unnecessarily duplicative programs and release promising ones for development or production. An especially important duty will be to analyze the technical programs of the military departments to make sure that an integrated research and development program exists to cover the needs of each of the operational commands. It will be his responsibility to initiate projects to see that such gaps as may exist are filled. In addition, the director will review assignments by the military departments to technical branches, bureaus and laboratories to assure that the research and engineering activities of the Defense Department are efficiently managed and properly coordinated. I would charge the director, under the direction of the Secretary of Defense, with seeing that unnecessary delays in the decision-making process are eliminated, that lead times are shortened, and that a steady flow of funds to approved programs is assured. Only under this kind of expert, single direction can the entire research and engineering effort be substantially improved. In these various ways, he should help stop the service rivalries and self-serving publicity in this area."