M. M. Snyder [*Physical Growth of California Boys and Girls from Birth to Eighteen Years* (Univ. of California Press, Berkeley, 1954), vol. 1, No. 2]. The Berkeley Growth Study sample was chosen from the same community, and at the same time (1928–29).

6. Initially, values were smoothed within the study if sample sizes at adjacent ages differed. For "mature height" values, Bayley's age-21 results are combined with values based on our own criterion of near-completion of skeletal growth (skeletal age 17.25 for boys, 16.25 for girls, as determined from application of Todd's standards to x-rays of the hand). The "birth" points include Bayley's 1-month data.
7. Any assertions of statistical significance in the text are based on designated tests and denote $P < .05$.
8. Since the father-child correlations are on the whole somewhat lower than the mother-child correlations, it should be noted that the reported heights of fathers may be somewhat more suspect than those of mothers. In addition to the possibility that paternity may have extended beyond the immediate family, the fact that, for a good portion of these data, the mothers reported both their own and their husband's heights is a source of possible inaccuracy. This is particularly true for the data beyond about age 6, and it is in these years, especially when the child reaches early adolescence, that between-parent differences in parent-child correlation are most marked. If mothers report their own heights more accurately than they report their husbands' heights, it may be that the father-child correlations are lower because of greater error in reported measurements. We have one datum which is somewhat reassuring. For 21 cases where fathers' heights were reported independently by both man and wife, the correlation between the two sets is .92, the distributions do not differ, and the correlations with children's heights are the same. Of course, fathers' heights may be less accurately reported by both parents; the likelihood that height is a more salient characteristic for males in our culture suggests such a possibility. However, reporting errors can hardly account for the sex difference in between-parent differential.
9. K. Pearson and A. Lee [*Biometrika* **2**, 237 (1903)] find correlations ranging from .49 to .51 for the four parent-child comparisons at approximate maturity. Their data are based on measurements for the oldest children over 18 years of age living at home in over 1000 English families. These results, which show higher correlations between father and child than our pooled data show, were obtained by correspondence and are based on measurements made by family members themselves in accordance with detailed written instructions. However, these correlations may somewhat underestimate the true values for that population. The Pearson and Lee sample, having reached adolescence at about the turn of the century, would, in many cases, not have attained their mature stature at the time of measurement. The authors themselves state that full height in this sample was not achieved until age 28 for men, age 25 for women. The parent-son correlations would therefore be more attenuated by this factor than the parent-daughter correlations; thus the equal correlations for the two sexes which Pearson and Lee report may be taken to suggest slightly higher correlations in height between sons and their mothers and fathers than between daughters and their parents.
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2 September 1962

X-Ray-Induced Chromosome Aberrations in the Corneal Epithelium of the Chinese Hamster

Abstract. When the corneal epithelium of the Chinese hamster is irradiated with ionizing radiation in vivo, a rectilinear relationship is observed between the yield of chromosome aberrations and the dose of x-rays within a dose range of 10 to 150 r. There is no threshold effect for chromosome breakage down to the 10-r level. The mean breakage rate of 0.00352 breaks per cell per roentgen is in very close agreement with the data obtained on other mammalian tissues, both in vitro and in vivo.

The study of chromosome aberrations is, at present, one of the most reliable methods of assaying radiation-induced cellular damage. The number of chromosome breaks constitutes a reasonably accurate biological dosimeter (*1*) and also serves as a fairly reliable indication of radiation-induced genetic damage in cases where other genetic assay systems are either impracticable or too cumbersome.

Since the initial findings of Muller (*2*) on the mutagenic effects of x-rays in *Drosophila* and parallel findings in plants by Stadler (*3*) and by Goodspeed and Olsen (*4*), a vast literature has been compiled concerning the production of radiation-induced chromosome aberrations. Sax (*5, 6*) made the first critically quantitative evaluation of radiation-induced chromosome aberrations. He found that in x-irradiated *Tradescantia* microspores one-hit aberrations increased approximately linearly with increasing dose and two-hit aberrations increased as the square of the dose if the duration of exposure was held constant. Carlson (*7*), working with the grasshopper *Chortophaga viridifasciata* and scoring only acentric fragments at late anaphase and telophase, observed that the number of single breaks in neuroblasts was proportional to the dose within a range of 7.8 to 125 r. Several workers (*8*), using genetic techniques to determine breakage in *Drosophila,* have demonstrated that one-hit aberrations increased linearly with dose and that two-hit aberrations increased exponentially and as the square of the dose at high dosage levels.

Recently, attention has turned to the study of the production of aberrations in mammalian cells. Several authors (*1, 9–11*) have studied metaphase aberrations in tissue culture. The frequencies of radiation-induced chromosome aberrations in vivo have been observed in the human (*1, 10, 12*), the monkey (*10*), and the Chinese hamster (*10, 13*).

Bender and Wolff (*14*), for example, have shown that x-ray induced chromosome aberrations in mammalian cells follow the same kinetics as aberrations studied in plants, and they feel that there is no reason to believe that there is a threshold at which aberration production begins. The purpose of the study reported here was to determine whether the linear relationship between aberration yield and dose holds good at low doses of x-rays in cells irradiated *in situ.* The studies in the work cited either were based on cells growing outside the body or did not conclusively establish a direct linear proportionality between x-ray dosage and chromosome breakage at low doses in mammalian tissue.

The experiments reported here were performed on the Chinese hamster, *Cricetulus griseus* (*15*), a rodent especially suitable for the purpose because of its low chromosome number ($2n = 22$) and the ease with which individual chromosomes can be distinguished.

All the hamsters used in the experiments were adult males. They were lightly anesthetized with ether and immobilized by a clamp-like device which fits over the nose and has two small plugs that are inserted into the ear sockets. All of the animals were given whole-body irradiation with x-rays at a dose rate of 10 r/sec, measured by a Victoreen dosimeter. The x-rays were generated by a General Electric x-ray unit (Maxitron 250) operated at 250 kv (peak) and 30 ma with a 1-mm aluminum filter.

The cytological method used in making the corneal epithelium preparations was a modification of that of Fechheimer (*16*). One hour and 40 minutes before the animals were sacrificed they received an intraperitoneal injection of 0.3 ml of a 1-percent colchicine solution. They were sacrificed, and the eyes were dissected out. The eyes were placed in a hypotonic saline solution (Hanks' basal saline solution without NaCl, 95 percent; Hanks' basal saline solution, 5 percent) and incubated at 37°C for 20 minutes. Cold, fresh alcohol–acetic acid (3:1) fixative was added, and the tissues were kept in the cold for an 18- to 24-hour

period. The eyes were then washed with distilled water, hydrolyzed in 1*N* HCl at 60°C for 8 minutes, and washed again with distilled water. The cornea was dissected out and placed in cold Feulgen stain. The corneal epithelium was then gently scraped off the cornea into a drop of 45-percent acetic acid on a clean slide and mounted according to the method of Ford and Hamerton (*17*).

Cells were selected for scoring under low magnification (150) and scored at a magnification of 1350. Whenever there was doubt concerning the existence of an aberration in a treated cell, the cell was scored as normal; whereas in the controls, such doubtful cases were scored as aberrations. Lesions in single chromatids which appeared to be achromatic lesions were not scored as aberrations.

Figure 1*A* shows the normal chromosome complement of the corneal epithelium of the Chinese hamster. Nearly all the metaphase preparations obtained with the corneal epithelium were of this high quality, indicating why this tissue is such fine cytological material for in vivo studies.

In 236 control cells scored, only two chromatid aberrations were observed. The spontaneous breakage rate was 0.0085 breaks per cell.

To determine the interval between treatment and fixation at which the maximum frequency of aberrations is observable, nine animals in groups of three were irradiated with doses of 50, 75, and 100 r, respectively, and sacrificed at 3-, 6-, and 12-hour intervals thereafter. When it was established that an interval of 6 hours between treatment and fixation yielded the highest frequencies for cell mitosis and chromosome aberrations, fixation was regularly carried out 6 hours after treatment for each dose (10, 25, 50, 75, 100, and 150 r). For two additional animals given doses of 10 and 25 r, respectively, fixation was carried out 3 hours after treatment.

At the 3-hour fixation time there were no mitoses for any of the doses studied except the 10-r dose. Even at that dose there was evidently some mitotic inhibition at 3 hours, since only 75 scorable metaphases were obtained from two animals as compared with the average of 150 to 200 metaphases per animal at the 6-hour fixation time. In the case of the 150-r dose, mitotic inhibition was observed up to 18 hours after treatment. At 18 hours

Table 1. Data on x-ray-induced chromosome aberrations in the corneal epithelium of the Chinese hamster in vivo. MI, Mitotic inhibition.

Dose (r)	Cells scored (*N*)	Chromatid deletions	Iso-chromatid deletions	Double-chromatid exchanges	Breaks	
					Per 100 cells	Per cell per roentgen ($\times 10^{-3}$)
0*	236	2	0	0	0.85	
			3-Hour interval			
10	75	3	0	0	4	3.15
25	MI					
50	MI					
75	MI					
100	MI					
			6-Hour interval			
10	177	8	0	0	4.52	3.67
25	100	6	1	1	9	3.26
50	100	11	3	2	18	3.43
75	100	17	1	4	26	3.36
100	100	25	4	4	37	3.62
150	MI					
			12-Hour interval			
50	90	3	0	1	5.55	0.94
75	100	6	3	0	9	1.09
100	100	7	3	0	10	0.92
			24-Hour interval			
150	150	13	13	6	25.33	
			30-Hour interval			
150	50	12	7	5	58	3.81

* Control.

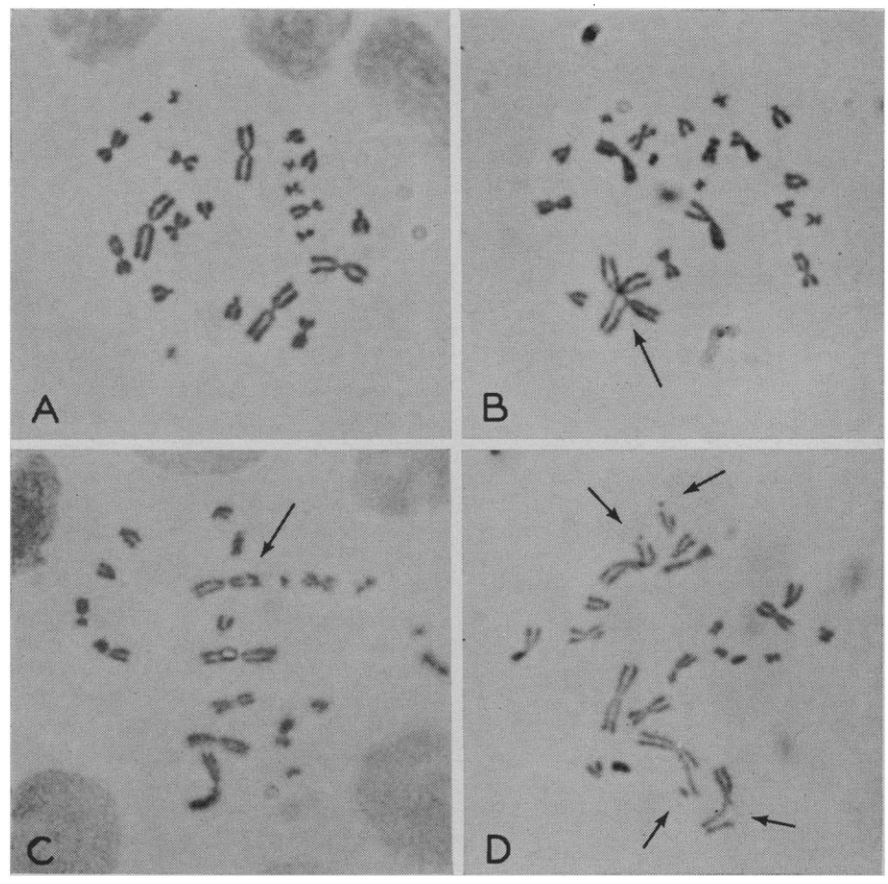

Fig. 1. Diploid corneal epithelium metaphases prepared by the method described in the text. *A*, normal metaphase from unirradiated control animal; *B*, cell with chromatid exchange; *C*, cell with isochromatid deletion; *D*, cell with four chromatid deletions. Some of the chromosomes of *B*, *C*, and *D* are not shown in the reproduction because they were distant from the main body of the chromosome complement.

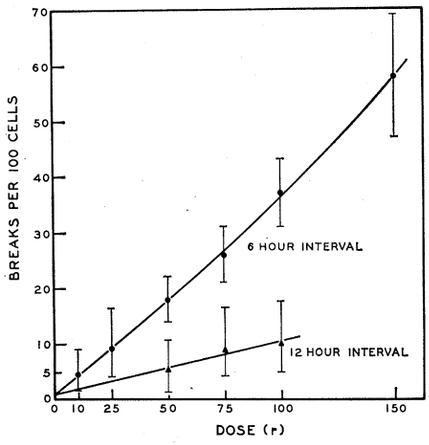

Fig. 2. X-ray-induced chromatid aberration frequencies in the corneal epithelium *in situ*. The measures of significance indicated for each point are the 95-percent probability limits, calculated according to the method of Stevens (*22*).

a small number of cells were observed in metaphase, but no mitotic burst occurred until 24 hours after treatment. However, the highest frequency of aberrations was observed 30 hours after treatment. Data for the cases in which the interval between treatment and fixation was 12 hours indicate that a marked decrease in the frequency of aberrations occurs between hours 6 and 12 after treatment.

Figure 1, *B*, *C*, and *D*, shows some of the typical chromatid-type aberrations observed. Table 1 summarizes the data obtained from all the treatments. A mean breakage rate of $(3.52 \pm 0.19)10^{-3}$ breaks per cell per roentgen was obtained for the corneal epithelium. This figure includes the data for the 6-hour fixation time for the 10-, 25-, 50-, 75-, and 100-r doses and the data for the 30-hour fixation time for the 150-r dose. At the 12-hour fixation time, for the three doses studied, a mean breakage rate of (0.95 ± 0.093) 10^{-3} breaks per cell per roentgen was obtained.

In these irradiated cells of the corneal epithelium of the Chinese hamster there is a direct linear proportionality between the dose and the yield of aberrations over the entire dose range studied, including the 10-r dose (Fig. 2). However, there is some indication that at the high dose (150 r) an exponential relationship begins to enter the dose curve, as expected, because of two-hit aberrations. The linear relationship at the lower dose levels (particularly at the 10-r dose) is of major interest since it signifies that there is no threshold effect down to the 10-r level. This rectilinear relationship at all dose levels with respect to point mutations and one-hit chromosome aberrations was predicted by Muller (*2*) and Sax (*5*), respectively, but the absence of a threshold for x-ray-induced genetic damage has been questioned by many people. Carlson's (*7*) findings in the grasshopper neuroblasts indicated that there was no threshold down to the 7.8-r level, but he was limited to scoring acentric fragments, and his findings did not answer questions pertaining to mammalian tissues. The data reported here, along with Bender's (*13*) findings of linearity between dose and yield of aberrations down to 25 r in the bone marrow of the Chinese hamster, Dubinin's (*18*) findings, and the recent work of Glass and Ritterhoff (*19*), seem to substantiate the view that there is no threshold for chromosome breakage down to the 5-r and 10-r levels.

The mean breakage rate of 0.00352 breaks per cell per roentgen obtained for the corneal epithelium is in very good agreement with the breakage rates obtained by Bender for human epithelioid cells in vitro (*9*, *10*), monkey epithelioid cells in vitro (*10*), human leukocytes in vitro (*1*), and human leukocytes in vivo (*20*) but is lower than the value obtained by Bender for Chinese hamster embryonic fibroblasts in vitro (*10*) and bone marrow cells in vivo (*13*). The differences in the data reported here and other available data on the Chinese hamster may be explained by the apparent instability of the chromosomes in embryonic fibroblast cultures, manifested in a high rate of spontaneous breakage; by differences in the interval of time between treatment and fixation; and by the qualities of the x-rays used in the studies of bone marrow and corneal epithelium. These are matters which more extensive investigation will clarify (*21*).

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General Disruption Resulting from Electrical Stimulus of Ventromedial Hypothalamus

Abstract. Electrical stimulation of the ventromedial nucleus of the hypothalamus caused hungry rats to stop eating. However, control tests showed such stimulation to be potentially noxious and capable of stopping drinking in thirsty rats. Thus the stopping of eating caused by this stimulation may not have been indicative of a primary effect on hunger.

In 1951 Anand and Brobeck (*1*) demonstrated that discrete bilateral electrolytic lesions in the region of the ventromedial hypothalamus resulted in hyperphagia, leading to obesity, whereas such lesions in the lateral hypothalamic region caused long-lasting aphagia and adipsia, leading to death.

The observation that the hunger drive can be elicited by appropriate electrical stimulation of the lateral hypothalamus is a consonant finding (*2*). Recently, the story seems to have been completed by reports that electrical stimulation in the medial hypothalamus of hungry animals inhibits eating (*3–5*). Other observations are reported here to emphasize the need for considerable care in assessing the significance of such an inhibition of eating.

Ten male rats of the Wistar strain were fitted with monopolar electrodes aimed bilaterally at the center of the ventromedial nucleus of the hypothalamus. With reference to the deGroot