RATIO OF THE SEXES IN THE OFFSPRING OF FEMALE AND MALE RATS IRRADIATED IN VARIOUS PERIODS OF THEIR ONTOGENESIS

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The question of the ratio of the sexes in the offspring of mammals born after the influence of ionizing radiations on sexually mature parents, has been the subject of many investigations, but the results of different authors differ. Thus, a substantial decrease in the number of male individuals has been obtained [16] among mice born as a result of crossings 5 to 18 days after irradiation. However, these data were not confirmed by subsequent studies. In experiments on the irradiation of male mice in doses from 400 to 1400 R [12, 17], no deviations in the numbers of males in the offspring of the irradiated male parents were obtained. Negative results have also been noted in a number of other investigations [13, etc.].

An extremely sharp change in the ratio of the sexes in the offspring (more than 85% males) occurred after total irradiation of the males and local irradiation of the testes of the rabbit in doses of 75 and 250 R [2, 3]. The author explains the predominance of males in the offspring [4, 5] by biochemical changes in the sperm, arising after x-ray irradiation.

The ratio of the sexes in the offspring of irradiated females has been the subject of a few investigations.

According to certain data [20], among the children whose fathers were subjected to radiation therapy without protection of the gonads (dose 721-1730 R) there were 55.5% boys (before irradiation 51.4%). The change in the ratio of the sexes in the offspring of irradiated fathers is explained by the appearance of sex-linked dominant lethal mutations.

In the already mentioned study [20], data are cited according to which there were fewer boys (46.3%) in the offspring of irradiated women in comparison with the corresponding control (55.1%). A study of the offspring of parents subjected to irradiation during the atomic bombardment at Hiroshima and Nagasaki [15] indicated a change in the ratio of the sexes, in a direction of a decrease in the number of boys among the offspring of mothers irradiated in doses from 100 to 400 R (the results approach statistical reliability). The changes in the ratio of the sexes are explained by recessive lethal sex-linked mutations.

The contradictoriness of the literature information on the variation of the ratio of the sexes in the offspring of irradiated animals served as the basis for conducting this investigation to determine the sex in the offspring after the irradiation of male and female germ cells in various pre- and postnatal periods of life of the parents.

PROCEDURE

The work was conducted on white rats of the Wistar line. In all the series of experiments, a single total irradiation was performed on the RUM-3 apparatus. Male and female fetuses 10, 12, 13, 15, 17, and 19 days of age were prenatally irradiated in a dose of 50 R. Newborn rats were irradiated postnatally at the ages 7, 14, 30, 45, 60, 75, and 90 days. The adult females were also irradiated in a dose of 600 R, and the males in doses of 600 and 1000 R. When sexual maturity had been reached, the irradiated females were mated with normal males and normal females with irradiated males. The sex was determined in 17-19 day fetuses according to the external appearance of the gonads of the latter, when the abdominal cavity was opened.

Ratio of the Sexes in the Offspring of Rats (Females and Males) Irradiated During Various Periods of Their Ontogenesis*

	Age of parent at time of irradiation	Stages of gametogenesis, state of gonads	Irradiation dose (in R)	Number of fetuses				ratio ♂/♀
				total	♀	♂	% ♀	
Females	10, 12, 13, 15, and 17 day fetuses	Migration and multiplication of oogonia	50	631	285	346	54,5 ± 1,9	1,21
	19 day fetuses, newborn	Premeiotic changes in nuclei of oocytes (from leptotene to diplotene stage)	50	288	145	143	49,6 ± 2,9	0,99
	7, 14, 20 day rats	Dictyotene. Beginning of growth of oocytes and formation of follicles	50	364	187	177	48,6 ± 2,6	0,95
	30, 40, and 45 day rats	Formation of multilayered and hollow follicles	50	437	227	210	48,1 ± 2,4	0,93
	50, 60, 75, 90 days and more	Structure of ovary characteristic of sexually mature females	50	257	142	115	45,5 ± 3,1	0,81
	Adult	The same	600	490	262	228	46,6 ± 2,3	0,87
Males	10-19 day fetuses and newborn	Migration and multiplication of primary germ cells (goniocytes)	50	537	279	258	48,0 ± 2,1	0,92
	7, 14, 30, and 45 day rats	Appearance (from 4th day) and multiplication of type A spermatogonia	50	513	261	252	49,1 ± 2,2	0,97
	60, 90 days and more	Sexual maturity	50	146	75	71	48,6 ± 4,1	0,95
	Adult	The same	600	217	107	110	50,7 ± 3,3	0,97
	Adult	" "	1 000	113	48	65	57,7 ± 4,6	1,35
Adult males and females were irradiated		" "	600	159	81	78	49,1 ± 3,9	0,96
Control		" "	—	269	139	130	49,4 ± 3,0	0,93

* The experiments were conducted from 1959 to 1963. Sex was determined in the 19 day fetuses of the first litter.

The data obtained were grouped in accord with the stages of gametogenesis and state of the gonads. In the females, the following periods were distinguished: a) migration and multiplication of oogonia (10-17 day fetuses); b) early premeiotic changes in the oocytes—from the leptotene to the diplotene stage of the prophase of meiosis (19 day fetuses and newborn rats); c) transition to dictyotene, or "resting" stage, as well as beginning of growth of the oocyte and formation of the follicles (7-10 day baby rats (7, 11]; d) formation of multilayered and hollow follicles and acquisition of a definitive structure by the ovaries (30-45 day baby rats); e) later stages, when the ovaries possessed the structure characteristic of sexually mature females. Grouping of the males was performed in accord with the periods: a) migration and multiplication of goniocytes (10-19 day fetuses, newborn rats); b) appearance (from the fourth day) and multiplication of type A spermatogonia and beginning of spermatogenesis (7-45 day baby rats); c) age (young and adult males) [10].

RESULTS

The results are presented in the table, from which it is evident that in the irradiation of female gametes (dose 50 R), with increasing age of the females, a tendency for an increase in the number of male individuals among their offspring is observed—from 45.5 to 54.5%. The difference between these values is statistically reliable (9.0 ± 3.6), but it proved unreliable in comparison with the control (5.1± 3.4 and 4.9± 4.2, respectively), perhaps on account of the insufficient number of fetuses investigated in the control. In the experiments on irradiation of females ranging in age from 19 day fetuses and newborn rats to 30-45 days of postnatal life, the number of male fetuses and their offspring was approximately the same as in the control. The numerical ratio of the sexes in the offspring was also unchanged as a result of irradiation of adult females in a dose of 600 R (difference in comparison with the control (2.8± 2.3).

Irradiation of the male gametes (dose 50 R) at various periods of pre- and postnatal life of the males revealed the same numerical ratio of the sexes in their offspring as in the control group of animals. Nor were the results changed when the adult males were irradiated in a dose of 600 R. Only in experiments on the irradiation of adult males in a dose of 1000 R was some predominance of males in the offspring obtained (57.5%). However, even here, the difference was statistically unreliable in comparison with the control (the difference between the percent of males in the experimental and in the control groups was 8.1± 5.5).

In the case of simultaneous irradiation of adult males and females in a dose of 600 R, followed by mating, the percent of male fetuses among their offspring did not differ from the control.

Thus, in experiments on the irradiation of female rats in various periods of their life, a statistically reliable increase in the number of males in the offspring was observed only among females irradiated in the prenatal period (10-17 day fetus) in a dose of 50 R. A slight predominance of males in the offspring was obtained in the case of irradiation of sexually mature males in a dose of 1000 R. In the case of such a high irradiation dose, dominant lethal mutations may arise, leading to an increase in the number of males in the offspring. The predominance of males obtained in the offspring of females irradiated in the prenatal period cannot be explained by dominant lethal mutations localized in the X-chromosome, since in this case the ratio of the fetuses should be unchanged. In the case of recessive sex-linked mutations and anomalies of meiosis, one might expect an increase in the percentage of females.

We turned our attention to the predominance of males in the offspring of irradiated females in connection with numberous literature data, cited in [1], on the study of the influence of external conditions on the determination of sex in Drosophila melanogaster. In particular, it was shown in the experiments of [1] that unfavorable influences on the parents (starvation, overheating, chilling, ether narcosis) give rise to a change in the ratio of the sexes, toward a predominance of males. The deciding factor in this case is the influence on the female. An analysis indicated that this is the result of the influence of the environment upon the female gametes in the proembryonic period. The maximum predominance of males in the offspring was observed when females were overheated for 2-4 days before laying eggs—during the critical period of development of the oocyte, in which the predetermination of sex is completed. During this period of oogenesis of Drosophila, the oocyte acquires the properties determining the greater probability of its combination with spermatozoa bearing the X- or Y-chromosome, and thereby, its subsequent conversion to male or female.

The question of the possibility of selectivity of fertilization has been discussed by many researchers [1]. A predominance of the male sex in the primary numerical ratio of the sexes has been established in man [19] and in the golden hamster [14, 18]. There are a number of indications of physiological differences in the sperm with X- and Y-chromosomes [8, 9]. It has also been demonstrated that in rodents the egg is nonpassive during the process of its combination with the sperm [6].

The increase in the number of males in the offspring of female rats irradiated in the prenatal period, obtained in our experiments, may be evidence that mammals (like Drosophila), which possess a homogamete female sex, are characterized not only by syngamy, but also by progamy of the sex determination; moreover, in mammals the predetermination of sex is accomplished at earlier stages of oogenesis during the period of multiplication of the oogonia.

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