VULNERABILITY OF NUCLEAR STRUCTURES OF THE MARROW CELLS OF MONKEYS TO RADIATION INJURY

L. P. Kosichenko

UDC 616.419-018.13-001.29-092.9

Recently discovered facts relative to the action of ionizing radiation on mammalian chromosomes have shown that ratiation damages the genetic material of the cell. As a rule the damage observed has been assessed by the time factor [1, 6], and no attempt has been made to study the relationship between the duration of the cell cycle and the quantitative degree of radiation injury to the chromosomes.

Experiments on monkeys, similar in their radiosensitivity to man as tissue culture experiments have shown [2, 5], are of great interest in the determination of the genetic dangers of ionizing radiation.

The object of the present investigation was to study the degree of vulnerability of the genetic structures of the marrow cells of monkeys to radiation injury and to determine the time during which the radiation injuries persist in a series of cell generations.

EXPERIMENTAL METHOD

The investigation was conducted on male macaques (Macaca mulatta) aged $2^1/_2$-3 years. Whole-body x-ray irradiation was applied to the monkeys in a dose of 100 R (voltage 180 kV, current 15 mA, filter 0.5 mm Cu and 1 mm Al, focus distance 150 cm, dose 2.8 R/min).

Material obtained 2 and 30 h, 5 and 15 days, and 3 months after irradiation was treated by the method described previously [3]. Altogether 5700 cells were studied. The mitotic index was expressed as the number of mitoses per thousand marrow cells.

EXPERIMENTAL RESULTS

The results showing the frequency of the nuclear disturbances and the mitotic activity of the marrow of the monkeys irradiated in a dose of 100 R are given in the figure. By comparison with the controls, in which the number of chromosomal aberrations was 0.5%, in the irradiated monkeys a marked increase in the number of chromosomal aberrations was observed, amounting to 70.1% e h after irradiation. This index showed a sharp fall 30 h after irradiation (21.6%), and the decrease continued until the fifth day. From then until the fifteenth day, the number of chromosomal aberrations remained unchanged, and a further decrease in their number to 1.5% took place only 3 months after irradiation, when it was still three times higher then the control level ($P = 0.035$). The high percentage (8%) of adhesions of chromosomes appearing soon after irradiation was also dependent on the time elapsing after irradiation.

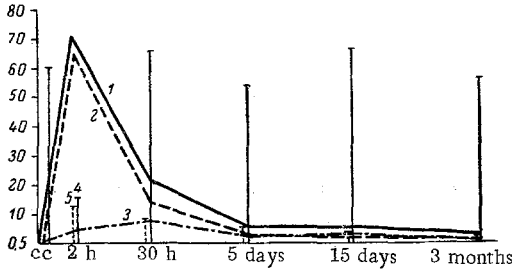
The results of the parallel study of the mitotic activity of the marrow cells in this particular variant of the experimental conditions revealed that the incidence of nuclear disturbances was inversely proportional to the mitotic activity. Two hours after irradiation (see figure), when the number of nuclear injuries in the cells was maximal, a sharp decrease in mitotic activity took place (60 mitoses in 1000 cells in the control compared with 15 in the experiment). Thirty hours after irradiation the mitotic activity had returned to the control level, at which it remained at all subsequent times of investigation.

The types of chromosomal aberrations in the marrow cells of the monkeys, like the incidence of the radiation injuries, depended on the time elapsing after irradiation (see table). Two hours after irradiation, for instance, chromosomal aberrations were found as a rule in the form of acentric fragments, the frequency of which was 65.7%; the incidence of bridges or centric fragments was 4.4%. A large proportion of the

Laboratory of Genetics, Institute of Experimental Pathology and Therapy, Academy of Medical Sciences of the USSR, Sukhumi. (Presented by Active Member of the Academy of Medical Sciences of the USSR, P. D. Gorizontov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 63, No. 5, pp. 101-104, May, 1967. Original article submitted May 15, 1965.

Distribution of Principal Types of Chromosomal Aberrations in the Bone Marrow Cells of Monkeys at Various Times after Irradiation (in %)

Time after irradiation	Number of cells	Chromosomal aberrations								
		single fragments	paired fragments	chromatid bridges	chromatid bridges with 1 fragment	chromatid bridges with 2 fragments	chromosome bridges	chromosome bridges with 1 fragment	chromosome bridges with 2 fragments	total number of aberrations,%
2 hours	1 000	52.4	13.3	2.1	1.6	0.7	–	–	–	70.1
30 hours	1 000	4.0	9.4	0.8	0.5	0.9	3.3	1.5	1.2	21.6
5 days	1 210	1.0	1.9	0.08	0.08	0.08	1.16	0.33	–	4.63
15 "	1 000	0.6	0.9	0.2	–	–	1.1	1.2	0.3	4.3
3 months	1 000	0.4	0.4	–	–	–	0.3	0.2	0.2	1.5



Nuclear disturbances and mitotic activity of the marrow of monkeys irradiated in a dose of 100 R. 1) Total number of chromosomal aberrations; 2) acentric fragments; 3) centric; 4) mitotic activity; 5) adhesion of chromosomes; C) control. Abscissa–time after irradiation; ordinate–nuclear disturbances and mitotic index.

acentric fragments consisted of single (52.4%) and paired (13.3%) fragments. All the centric fragments were chromatid bridges (4.4%; see table).

Thirty hours after irradiation the number of acentric fragments fell to one fifth of its value at the preceding investigation (13.4%), while the number of bridges was doubled (8.2%). The acentric fragments were distributed as follows: paired fragments 9.4%, single 4%. Meanwhile the chromosomal bridges (6%) were more numerous than the chromatid (2.2%).

The marked difference in the percentage of bridges and fragments found 2 h after irradiation subsequently decreased, and was no more than twice on the fifth and fifteenth day; 3 months after irradiation the difference had disappeared. Mainly paired fragments and chromosome bridges were seen 5 and 15 days, and also 3 months after irradiation. The number of single fragments varied within the control limits at these times. In the later periods (3 months) no chromatid bridges were present in the marrow cells of either the irradiated or the control monkeys.

Analysis of the results thus revealed the high sensitivity of the genetic structures of the marrow cells of the monkeys to ionizing radiation. Radiation aberrations were produced, and at the same time adhesion of the chromosomes and marked depression of mitotic activity took place. The phenomenon of the inverse relationship between the frequency of the nuclear disturbances and the mitotic activity in the early stages after irradiation has also been described for the bone marrow of mice [6].

The marrow cells of the irradiated monkeys fixed 2 h after irradiation belonged to the irradiated mitosis group [3]. At the time of irradiation these cells were in the postsynthetic phase, as shown by the predominance of single fragments, the presence of chromatid bridges, and the absence of chromosome bridges. Two hours later the mitotic activity of the bone marrow was sharply depressed, and it was restored to its original level 30 h after irradiation. Evidently the majority of marrow cells had started on the second mitosis at this time. This was in agreement with the author's earlier observations [3]. In the second mitosis in the marrow of the monkeys irradiated in a dose of 100 R the percentage of nuclear disturbances was reduced by two-thirds. In the next few generations, corresponding to a period of five days, the percentage of nuclear disturbances was reduced by more than three-quarters. The mitotic activity of the marrow remained within the control limits.

The results show that the marrow cells of the irradiated monkeys with the most severe nuclear damage are nonviable and die in the first cell generations. The chromosomal aberrations which are less

harmful for the organism may evidently survive and are transmitted to the next cell generations. A similar pattern of the dynamics of radiation injuries to the chromosomes has been described for the sex cells of monkeys [4]. The possibility also is not ruled out that the damage to the genetic material may persist for a long time in the reticular cells of the marrow, and that this damage may exert its effect on a series of cell generations.

LITERATURE CITED

1. Yu. S. Demin, Radiobiologiya, No. 4, 563 (1964).
2. N. P. Dubinin, Z. A. Dzhamilev, L. G. Dubinina, et al., in the book: Experimental Mutagenesis in Animals, Plants, and Microorganisms [in Russian], Vol. 2, p. 21.
3. L. P. Kosichenko and M. S. Bystrozorova, Radiobiologiya, No. 6, 818 (1964).
4. G. G. Tinyakov and M. A. Arsen'eva, Doklady Akad. Nauk SSSR, 122, No. 4, 589 (1958).
5. M. A. Bender, Proceedings of the Tenth International Congress of Genetics, Toronto (1959).
6. L. Karpfel, Folia Biol., Prahs, 7, 129, Prague (1961).