THE EFFECT OF X-RAY IRRADIATION UPON THE FORMATION OF A SYMPATHETIC NERVOUS SYSTEM MEDIATOR

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Penetrating radiation is known to affect the activity of the endocrine glands, including the function of the adrenal medulla [1, 4, 5, 10, 11, 17]. According to A. F. Maslova's data [12, 13], total x-ray irradiation causes phasic changes in the content of adrenergic substances in the blood and in the aqueous humor of the eye in rabbits: during the first seven minutes after irradiation, the content of these substances decreases, then, starting the eighth minute, increases until the end of the first day; starting the second day, there is a brief period when their content is normal, succeeded by a fresh increase one to two days before the animals' death. A. V. Tonkikh and Ts. L. Yankovskaya [15] indicate that acute depression of the adrenalin-secreting function of the adrenal glands in rats occurs eight days after total x-ray irradiation, succeeded by gradual normalization of this function. Small doses of ionizing radiation, however, can intensify the activity of the adrenal medulla [1].

These facts led us to investigate the formation of sympathin, a sympathetic nervous system mediator, in animals subjected to the influence of ionizing radiation; in previous papers, one of the authors of this article established that experimental resection of the adrenal medullas acutely disturbed the synthesis of sympathin in the operated animals [2, 3]. The immediate purpose of our investigation was to quantitatively determine the amount of the mediator sympathin liberated upon stimulation of the sympathetic nerves at different intervals after x-ray irradiation of the animals.

EXPERIMENTAL

The experiments were performed on frogs (Rana ridibunda), subjected once to total x-ray irradiation in a dose of 4500 r. Irradiation of the animals was carried out under the following conditions: RUM-3 apparatus, focal length 40 cm, voltage 160 kv, current 10 ma, no filter. The mortality of the irradiated frogs was considerably higher than that of the control group. The irradiated and control animals were kept under identical conditions. In some cases, dissection of the irradiated frogs revealed punctate hemorrhages in the internal organs.

The experimental object was the sympathetic innervation of the heart. The heart was isolated according to Straub and its cavities perfused with a Ringer's solution in a constant volume (0.5 ml). Sympathin was determined in the fluid extracted from the cardiac cavity before and after stimulation of the sympathetic nerve chain. The amount of the chemical mediator liberated during excitation of the sympathetic nerve fibers was determined by subtracting the mediator content of the perfusate obtained after stimulation of the nerves from that of the perfusate obtained before stimulation.

The K. V. Lebedev-S. V. Senkevich modification [9] of the method of luminescent analysis was used for quantitative determination of sympathin (adrenalin). We added 0.2 ml of the experimental perfusate to a quartz cuvette containing 5 ml of a 20 % solution of chemically pure alkali. The luminescence evoked by ultraviolet irradiation of the solution (a) was measured with a Pulfrich photometer. The luminous intensity of 0.2 ml of a standard solution (b) containing 5 μg adrenalin per 1 ml (dilution 1: 200 000) was determined under the same conditions.

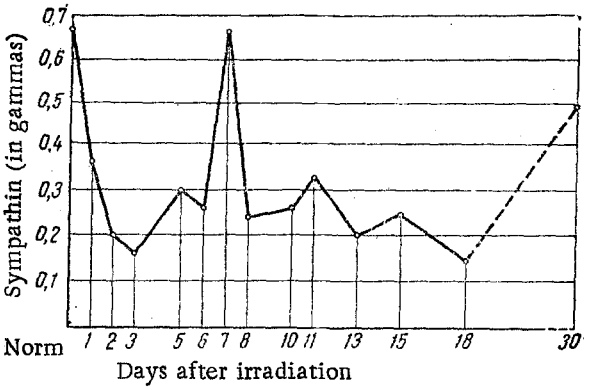
Under conditions of high dilutions, the intensity of a solution's fluorescent luminescence is known to be proportional to the solution's concentration. We therefore used the formula: $X = (a \cdot 5/b)$ (μg/ml) to compute the experimental solution's adrenalin content.

This method allowed us to assay the content of adrenalin and noradrenalin combined,(from their oxidation products) in the experimental perfusate,accurately to tenths of a microgram per 1 ml of solution.

RESULTS

We found either no sympathin at all or a content of less than 0.1 μg/ml in the fluid extracted from the cardiac cavity of a non-irradiated frog before stimulation of the sympathetic fibers. For all practical purposes, therefore, the sympathin content of the cardiac perfusate before stimulation of the nerves could be assumed to be zero. After stimulation of the sympathetic nerve chain, the perfusate acquired clearly expressed adrenergic properties. The average sympathin content of the perfusate at this time was found to be 0.65 μg/ml (13 experiments).

Phasic changes of the sympathin-forming function of the nervous system were observed in the frogs subjected to x-ray irradiation. Fifty experiments were performed on irradiated frogs. As in the case of the intact animals, the perfusates obtained from the hearts of the irradiated frogs before stimulation of the sympathetic nerve fibers did not contain sympathin. But the amount of sympathin liberated when the sympathetic nerve chain was stimulated at different intervals after irradiation was considerably changed by the influence of the latter. A reduced amount (averaging 0.15-0.28 μg/ml) was liberated during the first few days (2nd-4th days) after irradiation. From the fifth to the seventh day after irradiation, the sympathin-forming function of the autonomic nervous system was intensified. The average sympathin content of the cardiac perfusates collected during stimulation of the sympathetic nerves constituted 0.3-0.5 μg/ml, and in individual experiments, the amount of sympathin liberated equalled that in the non-irradiated frogs (0.65 μg/ml). On the 13th-18th day after irradiation, the sympathin-forming function again became depressed, as the reduced sympathin content of the cardiac perfusate indicated (0.2-0.15 μg/ml). The observations continued until the 30th day after irradiation. At this time, the amount of sympathin being liberated upon stimulation of the nerves had reached 0.5 μg/ml, indicating gradual normalization of the sympathin-forming process.



Changes in the sympathin content of perfusate extracted from the heart during stimulation of the sympathetic nerves at different intervals after x-ray irradiation of frogs.

Therefore, considerable changes in the formation of the sympathetic nervous system mediator,result from total x-ray irradiation; these changes are evidently due to disturbance of the hormonal function of the adrenal glands. The phasic changes in sympathin production by the nerve endings may be ascribed to the phasic nature of the change which researchers have observed [12, 13, 15], in the adrenalin-secreting function of the adrenal glands.

The graph shows the changes in the sympathin-forming function of the nervous system which we observed at various intervals after irradiation.

Experimental disturbance of sympathin synthesis effected by resection of the adrenal medullas is known to cause substantial disturbances in the activity of sympathetic innervation, particularly in the realization of the latter's trophic function [6, 7, 8 et al.]; the functional condition of the actual nerve conductors is also affected – lability decreases, and absolute and relative refractory phases in the postganglionic sympathetic nerve fibers increase in duration [14]. Similar functional changes in the sympathetic postganglionic fibers have been observed under the influence of radiation [11]. Therefore, one can assume that the disturbance of the sympathin-forming process,which we have established to occur under the influence of penetrating radiation,may be one of the causes for the changes in the functional condition of the sympathetic nervous system which a number of authors have observed during the development of radiation sickness [11, 16 et al.].

SUMMARY

A study was made of the extent of sympathin (a sympathetic nervous system mediator) liberation into the fluid perfused through the frog cardiac cavity at the moment of sympathetic nerves excitation. Sympathin (adrenalin) was determined by the method of luminescent analysis. As established, the total x-ray irradiation of frogs in a dose of

4,500 r disturbs the symphatin-forming process. On the 2nd-4th day after irradiation the amount of the sympathin liberated was found to be down and below its normal level; it almost regained from the 5th to the 7th day, but on the 13th-18th day experienced a new considerable drop. Only by the 30th day after irradiation there occurred a gradual normalization of the sympathin-forming process.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
