EFFECT OF IRRADIATION ON THE FORMATION OF HEMODYNAMIC PULMONARY EDEMA

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Experiments on 233 albino rats showed that large doses of ionizing radiation, causing marked leukopenia, increased the resistance of animals to pulmonary edema under the influence of adrenalin. This effect was particularly marked on the fourth day after irradiation. Relatively small doses (under 100 R) and also irradiation separately of the head, thorax, or abdomen, on the other hand, facilitated the development of pulmonary edema.

KEY WORDS: pulmonary edema; radiation sickness.

Ionizing radiation causes significant changes in the reactivity of the body and so affects the character of onset and the course of many forms of pathology [1, 2, 6-8]. However, the special features of formation of pulmonary edema after irradiation have not been investigated [4, 5]. The object of this investigation was to study the formation of acute hemodynamic pulmonary edema in the irradiated animal.

EXPERIMENTAL METHOD

Experiments were carried out on 233 albino rats distributed among the following series: to study the effect of whole-body irradiation on the formation of pulmonary edema – 34 animals, local irradiation 64; to study the time elapsing after irradiation 66 animals; and to study the dose of irradiation 69 animals. Irradiation was carried out on the RUM-II x-ray therapeutic apparatus or on the GUT ^{60}Co-400M apparatus. Local irradiation (of the head, thorax, abdomen, or whole trunk) was given by screening with lead plates, 10 mm thick, not covering the appropriate part of the body. Animals irradiated while completely screened served as the control. Hemodynamic pulmonary edema was produced by injecting adrenalin into the femoral vein in a dose of 0.02-0.03 mg/100 g body weight. This dose caused death of all the control animals 4-6 min after injection.

In the course of the experiments on the survival rate and life span of the animals the relative weight of the lungs (RWL) – the ratio between the weight of the lungs (in mg) and the body weight (in g) – and the dry residue of the lungs (in %) were determined. The index of edema fluid and the increase in blood volume of the lungs were determined by the method of Gaar and Seager [9]. The permeability of the air–blood barrier was investigated by means of Evans' blue, extracted from the lungs by Young's method [10].

EXPERIMENTAL RESULTS

On the fourth day after γ-irradiation in doses of 50 and 100 R the resistance of the animals to the endogenous action of adrenalin was lowered, as shown by the significant increase in RWL. With a further increase in the dose of irradiation, the survival rate of the animals with pulmonary edema began to increase ($P < 0.05$). The survival rate reached its maximum after irradiation in a dose of 800 R ($P < 0.001$). At the same time (judging from RWL) resistance to the formation of pulmonary edema increased significantly (Fig. 1).

An increase in the general resistance to adrenalin in rats irradiated in a dose of 800 R was observed as early as after 3-4 h ($P < 0.02$). By the fourth day resistance to the general toxic (as reflected in the survival rate $P < 0.001$) and to the endogenous (according to RWL) action of adrenalin reached a maximum, after which it declined (Fig. 2).

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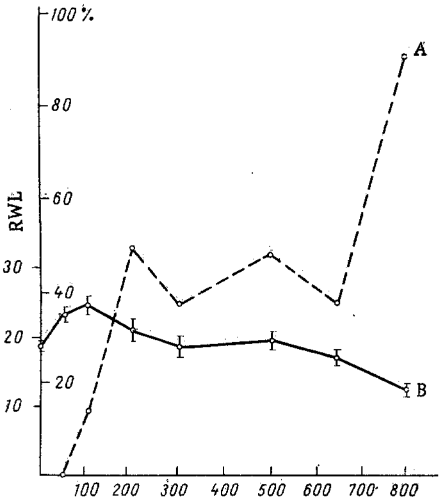

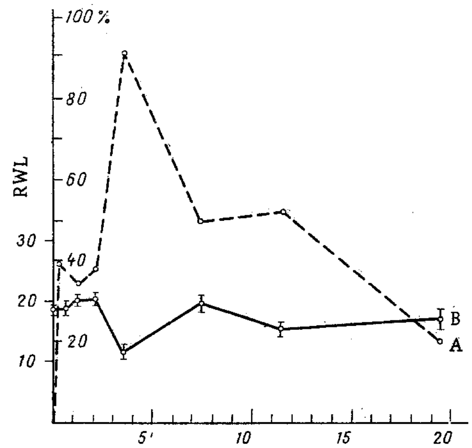

Fig. 1 | Fig. 2

Fig. 1. Changes in survival rate and relative weight of lungs of albino rats on fourth day after γ-irradiation during administration of adrenalin. Vertical axis – relative weight of lungs and survival rate; horizontal axis – dose of irradiation (in R). A) Survival rate after administration of adrenalin; B) RWL.

Fig. 2. Changes in survival rate (A) and relative weight of lungs (B) of albino rats during administration of adrenalin as a function of time elapsing after γ-irradiation in a dose of 800 R. Vertical axis – relative weight of lungs and survival rate; horizontal axis – days after irradiation.

TABLE 1. Changes in Indices of Adrenalin-Induced Pulmonary Edema (right lung) in Albino Rats on Fourth Day after Irradiation in a Dose of 700 R (M ± m)

Group of animals	No. of exp. animals	Number which died	Relative weight of lungs	Dry residue	Index of edema fluid	Increase in blood volume	Permeability of air–blood barrier (in mg Evans' blue/kg wet weight of tussue)
1) Irradiation with whole-body screening (control)	10	0	2,98±0,15	19,20±0,28	0,00±0,04	0,00±0,17	7,40±2,10
2) Irradiation with whole-body screening + adrenalin	8	8	11,13±0,64	13,53±0,39	3,35±0,36	4,79±0,37	77,75±6,60
3) Whole-body irrad.	8	0	2,85±0,25	19,60±0,19	–0,04±0,02	–0,09±0,24	14,44±4,60
4) Whole-body irradiation + adrenalin	8	2	7,07±1,26	15,94±1,48	1,60±0,65	2,50±0,86	24,54±13,10
P_{1-2}			<0,001	<0,001	<0,001	<0,001	<0,001
P_{1-3}			>0,05	>0,05	>0,05	>0,05	<0,05*
P_{2-4}			<0,02	<0,01*	<0,05	<0,05	<0,01
P_{3-4}			<0,01	<0,05	<0,05	<0,02	<0,05*

Legend. Asterisk denotes that P was calculated by the alternative variation method. When the dry residues were compared in groups 2 and 4 the number of variants above 14.25 was compared in each series, whereas when the indices were compared in groups 1 and 3 the number of variants above 13.2 was counted, and in groups 3 and 4 the number above 33.1.

All the subsequent experiments were carried out on the fourth day of acute radiation sickness caused by x-ray irradiation in a dose of 650-700 R. By this time the weight of the albino rats had fallen by 7.4% ($P < 0.001$) and the leukocyte count in the blood had fallen sharply (from 13.2 ± 0.78 to 0.9 ± 0.15 thousands/mm^3; $P < 0.001$). In the irradiated animals RWL was increased on account of increased filling of the blood vessels (Table 1), and the permeability of the air–blood barrier also was increased a little.

After injection of a dose of adrenalin lethal for all the control animals 75% of the irradiated rats survived. They developed less intensive pulmonary edema than animals protected against irradiation by screening, on account of a smaller increase in the blood volume in the lungs and a smaller disturbance of permeability of the air–blood barrier (Table 1).

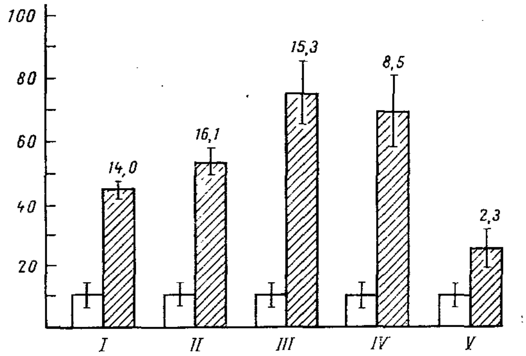

Fig. 3. Changes in permeability of air–blood barrier during adrenalin-induced pulmonary edema in control (I) and on fourth day after x-ray irradiation of head (II), thorax (III), abdomen (IV), or trunk (V) in a dose of 700 R. Unshaded column – before injection of adrenalin, shaded column – after injection of adrenalin. Vertical axis – quantity of Evans' blue (in mg/kg wet weight of tissue). Numbers above columns show number of leukocytes (in thousands/mm^3) on day of experiment.

The experiments with partial irradiation showed that the protective effect of whole-body irradiation was not due to the action of ionizing radiation on the head, the thorax with the forelimb, or the abdomen with the hind limb. All these variants of irradiation not only did not protect, but actually facilitated the development of adrenalin-induced pulmonary edema. In every case this was due to greater disturbance of the permeability of the air–blood barrier (Fig. 3), and in the case of irradiation of the abdomen, to a greater increase also in the blood volume of the lungs ($P < 0.01$). Under these circumstances symptoms of acute radiation sickness, including leukopenia, were absent on the fourth day after all these types of irradiation (Fig. 3).

Irradiation of the trunk with the limbs, like whole-body irradiation, sharply increased the survival rate of the animals after injection of a dose of adrenalin absolutely lethal for the control rats. These animals developed pulmonary edema less intensively because of the less marked disturbance of permeability of the air–blood barrier (Fig. 3) and the smaller increase in blood volume of the lungs ($P < 0.05$). Like whole-body irradiation, irradiation of the trunk with the limbs was followed by the development of a well-marked picture of acute radiation sickness, including leukopenia ($P < 0.001$; Fig. 3).

Large doses of ionizing radiation, causing marked leukopenia, thus increased the resistance of animals to the development of pulmonary edema under the influence of adrenalin. This effect is particularly marked on the fourth day. Small doses (under 100 R), and also irradiation separately of the head, thorax, or abdomen, on the other hand, facilitate the development of pulmonary edema. In experiments to study pulmonary edema following vagotomy and administration of chloramine [3], incidentally, an increase also was observed in the resistance of totally irradiated rats, but the increase was less marked.

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TEMPERATURE REACTION AND SURVIVAL OF EXPERIMENTAL ANIMALS AFTER MICROWAVE IRRADIATION

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In CBA mice and Wistar rats the diurnal dynamics of body temperature, the effect of keeping the animals in containers for irradiation, and the temperature reaction and survival of the animals after exposure to shf-fields of different intensities were investigated. The degree of elevation of the temperature and the survival rate of the animals were shown to depend on the power flux density and duration of exposure. The degree of elevation of the body temperature during irradiation and of its subsequent fall after irradiation can be regarded as prognostic signs of damage caused by the shf-field.

KEY WORDS: shf-field; body temperature; survival rate.

The study of the survival and temperature reactions of animals is necessary not only in the case of exposure to shf-fields of high intensity [1, 3, 5, 6], but also in connection with the development of methods of treatment and prevention of acute radio-wave lesions [2, 4]. However, the lack of a single methodological approach has led to disagreement in the interpretation of these indices. Some workers, for instance, consider that in acute radio-wave damage what is observed is mainly death "under the beam," and that animals which survive acute exposure do not die subsequently [3]. According to other investigators, moreover, death in the late periods after irradiation plays a significant role [2]. Investigations of body temperature are usually confined to the period of irradiation and do not extent to subsequent hours or days, although thermometric data are of considerable interest in the combined evaluation of the state of the body after exposure to microwave irradiation.

Accordingly the object of the present investigation was to study the temperature reaction and survival of experimental animals of different species after exposure to shf-fields of thermal intensities.

EXPERIMENTAL METHOD

Experiments were carried out on sexually mature CBA mice and Wistar rats. The body temperature and survival rate of the animals were studied for 30 days after a single exposure to microwaves (irradiation by the Luch-58 physiotherapeutic apparatus in the formed wave zone, with a frequency of 2375 MHz, power flux density (PFD) of 10, 40, and 60 MW/cm^2, exposures of 10, 30, 45, and 60 min, ambient air temperature 18-22°C, and relative humidity 60-75%). Irradiation was given in special containers made of radio-transparent material, and each animal was kept in an individual cage during irradiation. The rectal temperature was measured by a TPÉM-1 electrothermometer with skin detector before and at various times after irradiation.

The results were analyzed by the use of Student's criterion and methods of correlation and regression analysis.

EXPERIMENTAL RESULTS

During the day (from 9 a.m. to 4 p.m.) the body temperature of the mice fell on the average by 1.5°C, and considerable individual variations were observed. By contrast with the mice, the mean temperatures recorded in the rats were 36, 36.1, and 36.1°C at 9 a.m. and at 1 and 4 p.m. respectively.

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