Relationship among the Reaction of the Systemic Arterial Pressure, Constriction of Skeletal Muscle Arterioles, and Norepinephrine-Induced Changes in the Linear Blood Flow Rate in Rats Subjected to Whole-Body γ-Irradiation in a Dose of 1 Gy

A. G. Zakharov, L. S. Ivanov, E. V. Khmelevskii, V. K. Bozhenko, and A. M. Shishkin

UDC 615.357:577.175.523].015.2:615.849.1].015.4:616.1-008.1].076.9

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 117, № 3, pp. 274-277, March, 1994
Original article submitted December 26, 1993

The duration and amplitude of pressor reactions of AP to intravenous injection of norepinephrine remain unchanged 1, 3, and 5-6 days after irradiation. The duration of norepinephrine-induced changes in the diameter of arterioles of the thumb extensor muscle proper and the linear blood flow rate in them is decreased in irradiated animals.

Key Words: *ionizing radiation; norepinephrine; arterial pressure; arterioles of skeletal muscle*

Whole-body γ-irradiation in a dose of 1 Gy is now known to reduce the reactivity of arterioles in skeletal muscles to norepinephrine (NE) [3]. For the balanced operation of the circulatory system not only the amplitude characteristics but also the temporal relations between the processes occurring in the circulation are important.

The goal of the present study was to compare the temporal parameters of the general reaction of the circulatory system, evaluated from the changes in arterial pressure (AP), with the reactions of peripheral vessels in animals subjected to whole-body g-irradiation.

MATERIALS AND METHODS

Male Wistar rats weighing 200-320 g were irradiated with a dose of 1 Gy using a ROKUS-M γ-therapeutic apparatus. The reactions of systemic AP in the carotid artery and the reactions of microvessels in the extensor muscle proper of the thumb in response to 0.3, 1.0, and 3.0 μg/kg NE (Fluka) injected into the right jugular vein were recorded in acute experiments under urethane narcosis (1 g/kg i.v.) in control rats (n=6) and 1 (n=7), 3 (n=6), and 5-6 (n=5) days after irradiation.

The inner diameter and the linear blood flow rate were measured in the same part of the test arteriole by intravitam television microscopy. Second - and third - order arterioles were chosen, the central artery of the muscle being considered a first-order artery. The diameters of the microvessels were approximately 15-30 μ and did not differ statistically in any of the groups of animals. The statistical reliability of the differences was evaluated using the Student t test. The detailed technique was described earlier [3].

RESULTS

Figure 1 illustrates that 3.0 μg/kg NE injected intravenously induces a rise of AP (34±6% on av-

State Institute of Physical and Technical Problems; Research Institute of Diagnostics and Surgery, Moscow

0007-4888/94/0003-0277$12.50

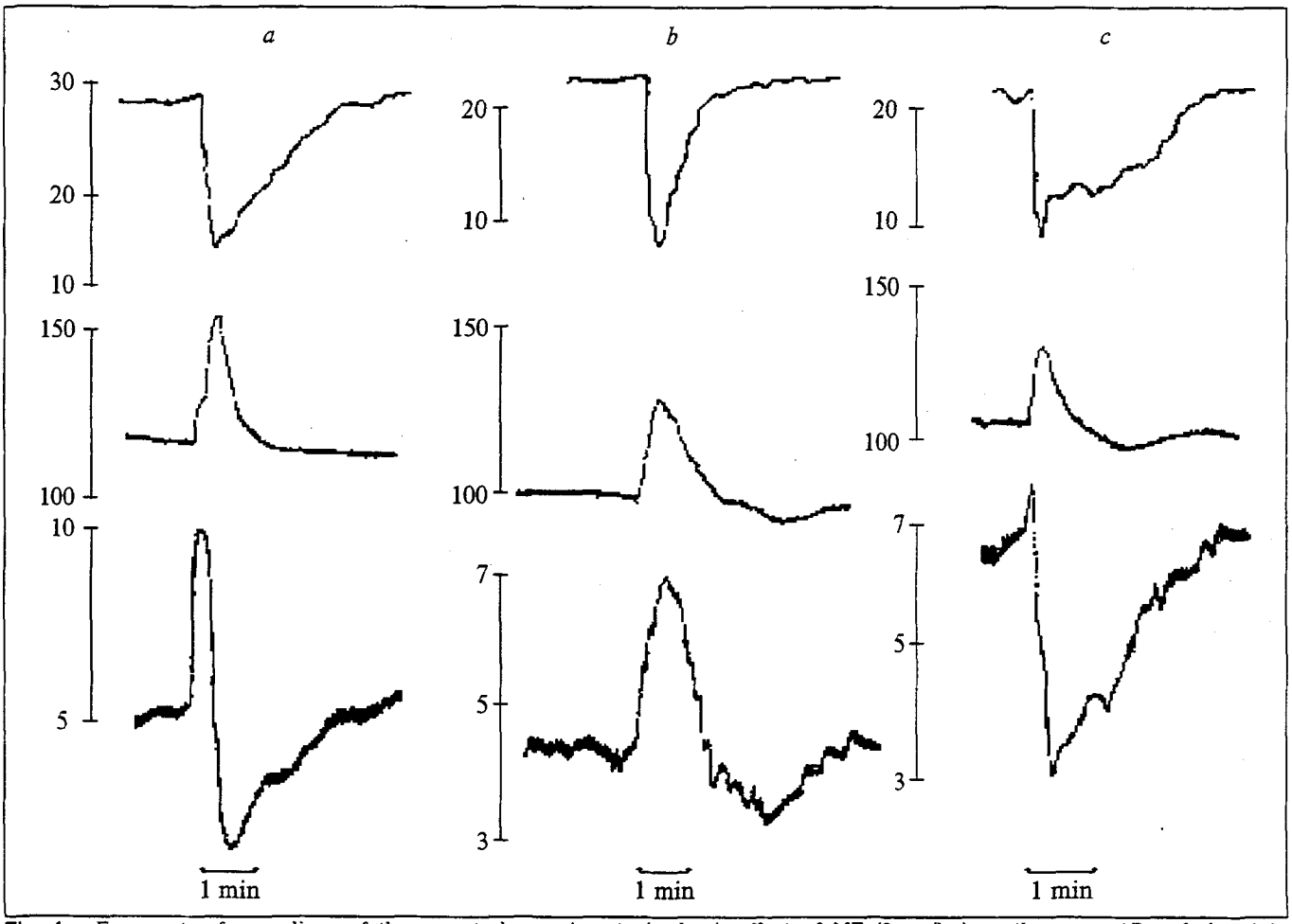

Fig. 1. Fragments of recordings of three control experiments (*a*, *b*, *c*): effect of NE (3 μg/kg) on the mean AP and the state of arterioles. From top to bottom: diameter of arterioles, μ; mean AP, mm Hg; linear blood flow rate, mm/sec.

erage) and a decrease of the inner diameter of arterioles (51.3±4.9% on average). The changes in linear flow rate induced by this and other doses in test arterioles do not differ much either in direction or in amplitude in different animals, which probably not only has to do with the local reaction of the test vessel but also reflects the state of a certain region of the vascular bed that is hemodynamically connected with the given microvessel. The fragments of recordings of three control experiments show that the reactions of AP are more transient in comparison with the prolonged chan-

TABLE 1. Duration (sec) of NE–Induced Reactions of AP (*tp*), Arteriolar Diameter (*td*), and Blood Flow Rate (*tv*) in the Control and at Different Times after Irradiation ($M \pm m$)

Experimental conditions	Dose, μg/kg								
	0.3			1.0			3.0		
	tv	*tp*	*td*	*tv*	*tp*	*td*	*tv*	*tp*	*td*
Control	72.5±12.0 (*n*=6)	134.0±18.4 (*n*=6)	116.4±10.5 (*n*=5)	68.0±6.5 (*n*=6)	131.0±24.0 (*n*=6)	97.0±21.3 (*n*=6)	103.0±19.9 (*n*=6)	194.0±25.1 (*n*=6)	162.0±28.0 (*n*=6)
Day 1	78.8±11.6 (*n*=8)	72.0±13.6* (*n*=6)	66.0±15.3* (*n*=7)	120.0±29.9 (*n*=8)	89.3±14.0 (*n*=8)	96.0±12.0 (*n*=7)	114.8±13.5 (*n*=8)	113.3±9.9* (*n*=8)	102.0±13.1 (*n*=8)
Day 3	79.5±16.3 (*n*=8)	73.5±16.1* (*n*=7)	96.0±21.2 (*n*=8)	102.8±17.0 (*n*=8)	111.8±16.4 (*n*=8)	115.8±32.2 (*n*=7)	128.0±23.2 (*n*=8)	129.8±17.1* (*n*=8)	108.0±32.2 (*n*=6)
Days 5-6	90.0±13.7 (*n*=6)	70.0±29.2 (*n*=5)	69.0±18.3* (*n*=6)	81.0±14.7 (*n*=6)	81.0±14.8 (*n*=6)	65.0±12.8 (*n*=6)	122.4±25.2 (*n*=5)	114.0±29.6 (*n*=5)	96.0±29.3 (*n*=5)

Note. * – $p<0.05$.

TABLE 2. Relative Duration of NE-Induced Reactions of Arteriolar Diameter (*td/tp*) and Blood Flow Rate (*tv/tp*) in Control Experiments and at Different Times after Irradiation ($M \pm m$)

Experimental conditions	Dose, μg/kg					
	0.3		1.0		3.0	
	td/tp	*tv/tp*	*td/tp*	*tv/tp*	*td/tp*	*tv/tp*
Control	2.05±0.43 (n=6)	1.69±0.22 (n=5)	1.99±0.38 (n=6)	1,46±0.32 (n=6)	2.09±0.36 (n=6)	1.82±0.44 (n=6)
Day 1	0.97±0.18* (n=7)	1.01±0.16* (n=6)	0.92±0.15* (n=8)	1.11±0.17 (n=7)	1.03±0.08* (n=8)	1.01±0.16* (n=6)
Day 3	0.99±0.12* (n=8)	1.14±0.23+ (n=6)	1.18±0.18 (n=8)	1.32±0.3 (n=7)	1.11±0.13* (n=8)	1.15±0.36 (n=5)
Days 5-6	0.84±0.28* (n=5)	0.88±0.08* (n=5)	1.09±0.24+ (n=6)	0.83±0.1+ (n=6)	1.23±0.22+ (n=5)	0.70±0.14* (n=4)

Note. * - $p<0.05$ (Student t test and U test), + - $p<0.05$ (U test).

ges in the diameter of arterioles and linear blood flow rate. Table 1 presents the duration of these reactions from the beginning to restoration of the initial value of the studied parameter in control and irradiated animals. We see from the table that the duration of reactions of AP in response to any dose of NE was less pronounced than the duration of the reactions of the linear flow rate in control animals; irradiation induced no statistically reliable changes in the duration of the reactions of AP; in the majority of experiments a marked tendency or a statistically reliable decrease was observed in the time of the reaction of the arteriolar diameter and linear blood flow rate in irradiated animals. This phenomenon becomes even more pronounced when the ratios of the duration of the reaction of both the arteriolar diameter and linear blood flow rate to the duration of the reaction of AP (*td/tp* and *tv/tp*, respectively) are calculated for each animal in each individual experiment (Table 2). In control experiments *td/tp* is about 2 and *tv/tp* ranges from 1.5 to 2, whereas in irradiated animals these parameters fluctuate around 1 and in the large majority of experiments they differ statistically from the control. These results suggest that in control animals the reactions of AP, arteriolar diameter, and linear blood flow rate start virtually simultaneously, with regard to AP propagation along vessels and to the latent period, but the peripheral reactions persist 1.5-2 times longer than the central ones. In irradiated animals both the AP and regional reactions with regard to the latent period occur practically simultaneously, but the duration of regional reactions is about half as long as that in the control animals.

γ-Irradiation in a dose of 1 Gy induces hypotension in irradiated rats one day after exposure, but not 3 and 6 days later. Neither the amplitudes [3] nor the duration of the pressor reactions of AP in response to any dose of NE are affected by irradiation, and no changes in the state of the circulation in skeletal muscle can be detected at any time. On the other hand, a stable and substantial reduction of spontaneous arteriolar vasomotion, implying a suppression of myogenic tonus, and a markedly reduced reactivity to any dose of NE at all times have been noted [3]. Moreover, irradiation leads to a marked shortening of the reactions of skeletal muscle arterioles to NE and marked alteration of their relations to systemic AP. Thus, the minor changes in the level of AP after irradiation and the absence of changes in its pressor reactions do not reflect marked alterations of myogenic tonus and regulation of skeletal muscle arterioles. In view of the well-known differences in magnitude of myogenic tonus [7] and reactivity to catecholamines [4] in various circulatory regions, this phenomenon may be explained by an altered distribution of the minute volume in irradiated rats in the course of regulatory reactions, i.e., premature (in comparison with controls) restoration of the circulation in skeletal muscle after vasoconstriction may occur due to blood supply from other vascular regions, resulting in maintenance of the reactions of systemic AP.

A comprehensive study of patients with vasoregulatory asthenia (VRA) [6] led to the conclusion that a pronounced drop of myogenic tonus of the arterial bed in skeletal muscles represents the leading component in the development of this disease. The signs of VRA are similar to those of the neurocirculatory dystonia exhibited by persons who had been exposed to low doses of ionizing radiation in the Chernobyl accident [2,5]. Comparing the above data [2,5,6] and our results, we proposed that low doses of radiation are able, through sup-

pression of the myogenic tonus and disturbed regulation of microvessels in skeletal muscles, to induce a complex of circulatory symptoms characteristic for neurocirculatory dystonia.

REFERENCES

1. E. V. Gubler and A. A. Genkin, *Use of Nonparametric Statistics in Medico-Biological Experiments* [in Russian], Leningrad (1973).
2. P. V. Voloshin, T. V. Kryzhenko, T. S. Mishchenko, *et al.*, in: *Radiation Injuries and Prospects of Individual Protective Gear against Ionizing Radiation* [in Russian], Moscow (1992), pp. 67-70.
3. A. G. Zakharov, L. S. Ivanov, E. V. Khmelevskii, and V. K. Bozhenko, *Byull. Eksp. Biol. Med.*, **114**, № 10, 355-357 (1992).
4. V. A. Levtov, *Chemical Regulation of Regional Circulation* [in Russian], Leningrad (1967).
5. V. V. Muskatin'ev, G. K. Tsinkina, A. I. Shishkin, and V. A. Lun'yakov, in: *Radiation Injuries and Prospects of Individual Protective Gear against Ionizing Radiation* [in Russian], Moscow (1992), pp. 70-72.
6. K. Graf, *Grosse und Reagibilitat der Extremitatenduchblutung bei Vasoregulatorischer Asthenie*, Uppsala (1966).
7. H. D. Green and C. E. Rapela, *Circulat. Res.*, № 14, 15, Suppl. 1, 11-16 (1964).

MICROBIOLOGY AND IMMUNOLOGY

Regulation of the Adenylate Cyclase System in the Lungs of Rats Treated with Plague Toxin

T. D. Cherkasova, V. A. Yurkiv, and V. I. Pokrovskii

UDC 616.24-022.7:579.843.95]-092.9-07

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 117, № 3, pp. 278-280, March, 1994
Original article submitted November 5, 1993

It is demonstrated that the "murine" lethal toxin of *Yersinia pestis* desensitizes the β-adrenergic receptors coupled to the pulmonary adenylate cyclase system. The degree of adenylate cyclase activation in rat pulmonary membrane preparation by isoproterenol or histamine and the number of β-adrenergic receptors decrease after a 2-h incubation with the toxin.

Key Words: *plague toxin; adenylate cyclase; rat lungs; β-adrenergic receptors; histamine H_1 receptors*

Experimental intoxication with the bacteria *Yersinia pestis* and their toxins leads to the development of respiratory insufficiency, inflammation, and edema with a high occurrence of lung tissue necrosis [3,5]. The mechanisms underlying these processes have been insufficiently investigated. It is known that hormones and biologically active substances (catecholamines, acetylcholine, serotonin, and histamine) play an important role in lung physiology. They regulate the airway and vascular tone, vascular permeability for electrolytes and water, and the synthesis and secretion of mucus and surfactant via the corresponding receptors coupled to the adenylate cyclase (AC) and Ca-mobilizing systems [9].

In this work we studied the regulatory properties of pulmonary AC and the number of β-adrenergic and histamine H_1 receptors in rats treated with the *Yersinia pestis* toxin.

Central Institute of Epidemiology, Moscow

0007-4888/94/0003-0280$12.50