CHANGES IN REACTIVITY OF RECEPTORS OF SMALL INTESTINE IN DOGS WITH ACUTE RADIATION SICKNESS

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UDC 617-001.28-036.11-092.9-07:616.
341-056-072.7

Whole-body x-ray irradiation (500 R) of dogs causes an increase in the reactivity of the cholinergic and a decrease in reactivity of the serotoninergic receptors of the isolated Thiry-Vella loop of intestine. Irradiation of the animals had no significant effect on the reactivity of the adrenergic receptors.

The information on changes in the reactivity of adrenergic, cholinergic, and serotoninergic intestinal receptors in radiation sickness available in the literature is very incomplete and contradictory. Some workers, for instance, describe an increase in the sensitivity of cholinergic structures [3-7, 9], while others observe a decrease [2, 8], and a third group finds no change whatever in their functional state [10]. The same applies to adrenalin: sensitivity to it is described as being increased [2, 5] or unchanged [8]. So far as the reactivity of serotoninergic structures is concerned, its increase has been reported [1, 4].

It must also be noted that the data in the literature are difficult to compare since the experiments were carried out on animals of different species and under different conditions. Nevertheless, the elucidation of this problem is extremely important because the mechanisms of the "intestinal syndrome" play an important role in the pathogenesis, course, and outcome of radiation sickness.

The investigation described below was accordingly carried out to study the state of the adrenergic, cholinergic, and serotoninergic structures of the intestine of dogs with acute radiation sickness.

EXPERIMENTAL METHOD AND RESULTS

Chronic experiments were carried out on six watchdogs with intestinal loops isolated by the Thiry-Vella method. The intestinal movements were recorded graphically with the aid of an inflated balloon (volume 2 ml). The pharmacological agents were injected into a leg vein in the following concentrations: adrenalin and carbachol 0.001%, serotonin 0.01%.

After the establishment of threshold and suprathreshold doses of the mediators the animals were totally irradiated with x rays in a dose of 500 R (187 kV, 15 mA, filter 0.5 mm Cu, distance 100 cm, dose rate 12.5 R/min, duration of irradiation 40.6 min). The experiments were carried out as a rule on fasting animals 18-20 h after the last meal. The severity of the radiation sickness was assessed hematologically.

Whole-body x-ray irradiation in a dose of 500 R did not significantly alter the response of the intestine to adrenalin. Very slight changes were observed only on certain days, and the suprathreshold effects remained constant at all times of testing. For a period of two weeks after irradiation the responses to adrenalin were little different from initially. Only in one experiment (on the 15th day) was an increase in the response threshold observed. In this case, also the suprathreshold dose inhibited intestinal contractions, just as it did before irradiation. Observations during the next two months showed no appreciable changes in the responses of the intestine to adrenalin.

(Presented by Academician of the Academy of Medical Sciences of the USSR S. V. Anichkov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 75, No. 3, pp. 48-51, March, 1973. Original article submitted December 14, 1971.

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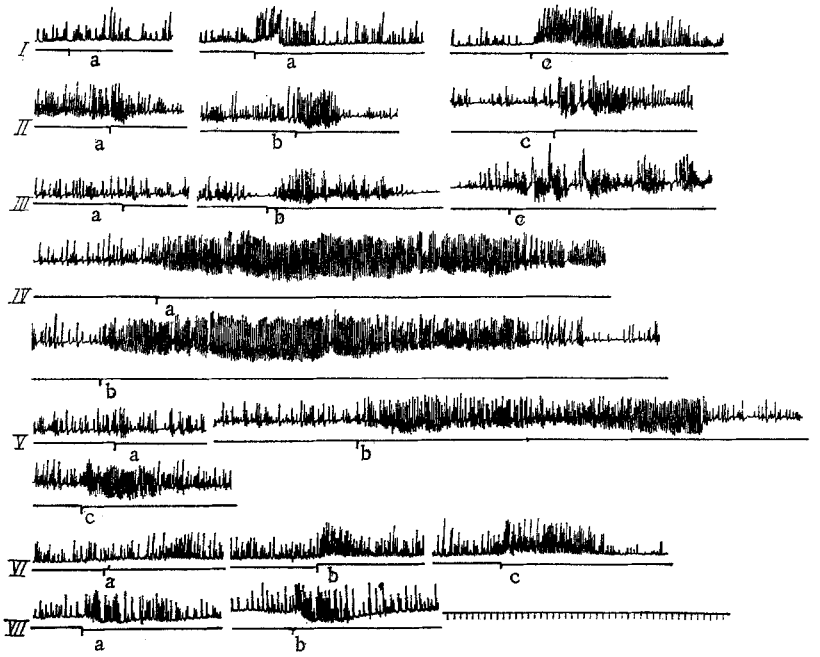

Fig. 1. Responses of intestine to injection of carbachol in the dog Ryzhik before irradiation (I) and 1 (II), 3 (III), 5 (IV), 12 (V), 20 (VI), and 25 (VII) days after irradiation. Doses of drug injected: a) 0.6 μg/kg; b) 0.12 μg/kg; c) 0.18 μg/kg. Here and in Fig. 2, from top to bottom: intestinal movements, marker of stimulation, time marker (15 sec).

Unlike the adrenergic structures, the state of the cholinergic receptors underwent substantial changes in the course of radiation sickness. The sensitivity of the intestine to carbachol was considerably increased throughout the period of investigation (40–50 days), starting on the second or third day after irradiation. The results of experiments on one of the dogs are shown in Fig. 1 as an illustration. By the third day after irradiation the reactivity of the intestinal cholinergic structure was sharply increased. In a dose which before irradiation was above the threshold (0.6 μg/kg) carbachol appreciably activated intestinal movements. Injections of carbachol in a dose of 0.12 μg/kg led to a prolonged motor effect. Strong and prolonged responses occurred during the subsequent periods of observation. Increased reactivity of the cholinergic structures of the intestine persisted for 50 days after irradiation. It must also be noted that paradoxical relations between dose and effect developed during radiation sickness, for a smaller dose led to the appearance of a stronger response (Fig. 1). The results obtained on the other dogs were quite indistinguishable from that described above.

Whereas the reactivity of the cholinergic intestinal structures was sharply increased after irradiation, their sensitivity to serotonin was considerably reduced. In the dog Yula, for instance, before irradiation injection of serotonin in a dose of 5 μg/kg was threshold, while injection of 7 μg/kg always led to a clearly marked effect (Fig. 2). These responses were somewhat weakened actually on the day of irradiation. By the third day none of the above doses was effective and only when injected in a dose of 20 μg/kg did serotonin stimulate intestinal movements. Until the end of the first week the sensitivity of the serotoninergic structures was sharply inhibited. Later, on the 7th day, the response thresholds were restored, while later still they increased once again (Fig. 2).

The results of these chronic experiments showed that in the course of radiation sickness the sensitivity of the intestine to adrenalin undergoes no significant changes. Information in the literature indicating increased sensitivity to the intestine to adrenalin is difficult to reconcile with the results described above. The explanation evidently lies in the different experimental conditions, for acute experiments were performed on isolated segments of intestine from frogs, mice, rats, and guinea pigs. In addition, not all investigators have observed changes in the sensitivity of the adrenergic receptors in small animals.

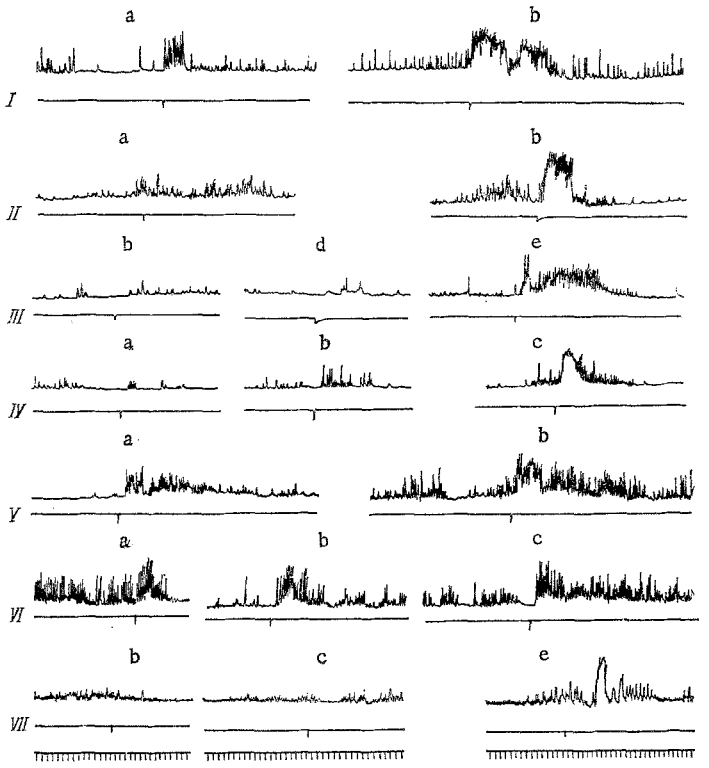

Fig. 2. Responses of intestine to injection of serotonin in the dog Yula before irradiation (I) and 1 (II), 3 (III), 5 (IV), 7 (V), 9 (VI), and 14 (VII) days after irradiation. Doses of drug injected: a) 5 μg/kg; b) 7 μg/kg; c) 10 μg/kg; d) 15 μg/kg; e) 20 μg/kg.

With respect to cholinergic systems the facts described above are in agreement with those in the literature indicating an increase in their sensitivity after irradiation in rats, mice, and frogs. These results do not in any way question the view that in radiation sickness there is a definite increase in the excitability of the muscarinic cholinergic systems of the intestine, which persists for a long period of time (up to 1.5 months).

The results of these experiments suggest that an important role in the mechanisms of the disturbances of intestinal movements in radiation sickness is played by disturbances of the parasympathetic division of the autonomic nervous system.

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