

CHANGES IN AGGREGATION OF PLATELETS CAUSED BY SEROTONIN AND ADP IN ACUTE RADIATION SICKNESS

V. M. Dorofeev, V. M. Zyablitskii,
and G. V. Nestaiko

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Aggregation of platelets produced by serotonin and ADP was studied in experiments on rabbits in the healthy animals and at various times after irradiation in a dose of 600 R. Aggregation of platelets by the action of ADP is reduced 1, 7, and 15 days after irradiation, and the platelet aggregates become less stable. Aggregation of platelets by serotonin is reduced only at the height of radiation sickness (7th day). It is considered that the disturbance of the aggregating power of the platelets by serotonin is due to a decrease in the number of "5-HT-receptors" or to qualitative changes in them.

Besides the thrombocytopenia, another factor of great importance in the pathogenesis of the radiation hemorrhagic syndrome is a disturbance of platelet function [1, 7]. Aggregation of platelets takes place by the action of ADP, thrombin, catecholamines, serotonin, and various other substances [6, 8, 9]. In acute radiation sickness the aggregating properties of the platelets are reduced by the action of ADP [2].

The object of the present investigation was to compare the effects of ADP and serotonin on aggregation of the platelets in acute radiation sickness.

EXPERIMENTAL METHOD

In experiments on 35 chinchilla rabbits of both sexes, weighing 2.6-2.9 kg, the animals received a single dose (600 R) of whole-body irradiation by Co^{60} γ -rays (dose rate 125 R/min). By means of a silicone-treated needle, 35-40 ml blood was taken from the heart of the animals 1, 7, and 15 days after irradiation and from healthy animals. The blood was mixed with 3.8% sodium citrate solution in the ratio 9:1. Plasma rich in platelets was obtained by centrifuging the blood at 120 g for 10 min. The number of platelets in the plasma was determined by a phase-contrast method [4]. Aggregation of the platelets was investigated by Born's method [3]. The process of aggregation of the platelets was recorded for 15 min when the platelet count was $2 \times 10^5/\text{mm}^3$ plasma and the final concentrations of ADP and serotonin were 0.2 mg/ml (1st test) and 10 $\mu\text{g}/\text{ml}$ (2nd test) respectively. Aggregation of the platelets of each animal was recorded simultaneously in both tests. The intensity of aggregation (decrease in optical density of the aggregating platelet suspension, expressed in millivolts) and the percentage deaggregation were recorded. The results were subjected to statistical analysis by Student's t criterion.

EXPERIMENTAL RESULTS

The intensity of aggregation of platelets from the healthy donors by serotonin was on the average 84% below the intensity of aggregation produced by ADP (Table 1; Fig. 1). The platelet aggregates obtained by the effect of serotonin in all cases underwent deaggregation. The platelet aggregates obtained

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TABLE 1. Aggregation of Rabbit Platelets at Different Stages of Acute Radiation Sickness ($M \pm m$)

Time of investigation (days)	Number of animals	Serotonin		ADP	
		intensity of aggregation	percent of deaggregation	intensity of aggregation	percent of deaggregation
Before irradiation	11	$0,78 \pm 0,07$	100	$3,02 \pm 0,19$	18
1st	7	$0,75 \pm 0,11$	100	$2,20 \pm 0,29^1$	0
7th	9	$0,39 \pm 0,04^1$	100	$2,40 \pm 0,23^1$	44
15th	8	$0,65 \pm 0,07$	100	$2,37 \pm 0,22^1$	75

¹P < 0.05 compared with initial value.

by the action of ADP were more stable: deaggregation took place in only two of 11 cases and it was incomplete.

On the 1st day after irradiation the intensity of aggregation of the platelets under the influence of ADP showed a significant decrease, whereas aggregation by the action of serotonin was unchanged. However, at the height of the radiation sickness (on the 7th day) the ability of the platelets to aggregate under the influence of serotonin was disturbed by a greater degree (by 50%) than under the influence of ADP (by 24%). On the 15th day after irradiation the ability of the platelets to aggregate by the action of serotonin was restored, whereas their aggregation under the influence of ADP remained below its initial value, and the percentage of deaggregation was increased by four times.

Unlike ADP, serotonin is known to induce only the first phase of platelet aggregation, and this is usually followed by a phase of deaggregation [3]. This may account for the differences between the reactions of the platelets of the irradiated animals to serotonin and ADP.

The phenomenon of reduced aggregating power of the platelets under the influence of serotonin is itself of considerable interest. Relatively recent investigations have shown that aggregation of platelets under the influence of serotonin is dependent on the state of their membrane structures known as 5-HT-receptors [5]. The decrease in aggregation of the platelets of irradiated animals under the influence of serotonin may therefore indicate changes in the number or quality of these membrane structures.

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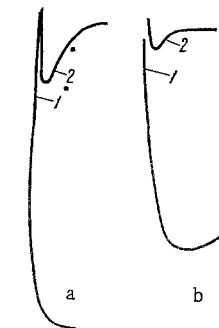


Fig. 1. Aggregation of platelets by ADP (1) and serotonin (2) in healthy rabbits (a) and on 7th day after irradiation (b).