

CONNECTION BETWEEN THE SEROTONIN LEVEL
IN THE BLOOD AND INTESTINE AND ACTIVITY
OF FACTOR XIII IN ACUTE RADIATION SICKNESS

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Intravenous injection of factor XIII, unlike other plasma components, at the height of acute radiation sickness in rats increases the serotonin concentration in the blood and duodenum.

The bleeding tendency in radiation sickness is largely due to a decrease in the activity of factor XIII in the blood [1, 2], so that the functions of the platelets (adhesiveness and aggregation) and the resistance of the vessel walls are disturbed [3]. Intravenous injection of factor XIII into rats, guinea pigs, and rabbits at the height of acute radiation sickness restores the platelet functions to normal, increases vascular resistance, and reduces the bleeding tendency [4, 7, 10]. A decrease in the activity of factor XIII is also characteristic of diatheses induced by factors other than radiation [5, 20], in which the blood and tissue serotonin level is low [14, 19, 21, 23]. Great importance in the pathogenesis of the hemorrhagic syndrome in radiation sickness, in which the ability of the platelets to adsorb and synthesize serotonin is disturbed [13], is attached to the fall in the serotonin level [11, 12, 15].

Reduction of the bleeding tendency as a result of transfusions of factor XIII in irradiated animals renders the study of the blood and tissue serotonin concentrations under these conditions a matter of urgency, and the investigation described below was carried out for this purpose.

EXPERIMENTAL METHOD

Experiments were carried out on 62 Wistar rats of both sexes weighing 200-300 g. The animals were irradiated with Co^{60} γ -rays in a dose of 600 R (dose rate 50 R/sec). At the height of radiation sickness 16 animals were given an intravenous injection of factor XIII, 18 animals received preparations of fibrinogen containing traces of factor XIII, and 16 animals received preparations of a mixture of low-molecular-weight fractions not containing fibrinogen or factor XIII, in a dose of 40 mg protein/kg body weight, made up in a volume of 3.8 ml/kg body weight. Control animals (12 irradiated rats) received injections of the corresponding volumes of physiological saline (pH 7.2).

The preparations were obtained from the plasma of healthy Wistar rats by gel-filtration through Sephadex G-200 (particle size 40-120 mesh), followed by removal of salt and lyophilization. The concentration of serotonin in the preparations did not exceed $0.1 \mu\text{g/ml}$. Addition of 0.05 ml of the factor XIII preparation to 1 ml platelet-free plasma obtained from an animal at the height of acute radiation sickness restored the activity of factor XIII to the level in healthy animals.

The vascular resistance [8], bleeding time [18], volume of the blood loss (from the hemoglobin concentration in the outflowing blood), and the concentration of serotonin in the blood and duodenum [22] were determined 60 min after the transfusions. The numerical results were analyzed by statistical methods [9].

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TABLE 1. Serotonin Level ($M \pm m$) in Blood and Duodenum of Rats at the Height of Acute Radiation Sickness 60 min after Intravenous Injection of Plasma Components of Healthy Animals

	Before injection	After injection of plasma components			
		factor XIII	fibrinogen	without fibrinogen and factor XIII	physiological saline
Blood (in $\mu\text{g/ml}$)	0.10 ± 0.02	$0.25^1 \pm 0.04$	0.19 ± 0.03	0.10 ± 0.03	0.11 ± 0.03
Duodenum (in $\mu\text{g/g}$)	4.45 ± 0.26	$5.80^1 \pm 0.19$	4.62 ± 0.26	4.12 ± 0.21	4.64 ± 0.33

¹ $P < 0.05$

EXPERIMENTAL RESULTS

All the irradiated animals developed moderately severe acute radiation sickness: on the 8th day of the disease the platelet count in the blood was reduced to $216,000 \pm 17,000$ per mm^3 (compared with $700,000 \pm 26,000$ per mm^3 before irradiation), the blood serotonin level was reduced by two-thirds, the serotonin concentration in the duodenum was reduced from 5.14 ± 0.47 to $4.45 \pm 0.26 \mu\text{g/g}$, the vascular resistance was lowered, and the bleeding time and volume of the blood loss were increased.

Injection of factor XIII increased the vascular resistance from degree IV to I and restored the normal bleeding time and volume of the blood loss. Transfusions of other plasma components had no hemostatic effect.

The results in Table 1 show that injection of factor XIII at the height of acute radiation sickness caused an increase in the serotonin concentration in the blood and duodenum. Transfusions of other plasma components and of physiological saline had no effect.

Elevation of the serotonin level after transfusions of factor XIII in irradiated animals undoubtedly contributes toward the decrease in bleeding tendency [17]. It can also be assumed that serotonin participates in the reduction of the bleeding tendency in patients treated with preparations containing factor XIII for a deficiency of this procoagulant [16]. The concentrations of serotonin and factor XIII are not mutually dependent in acute radiation sickness, for intravenous injection of serotonin at the height of the disease has no effect on the activity of factor XIII or on the quality of the fibrin clot [6]. Injection of factor XIII in acute radiation sickness probably increases the ability of the platelets to adsorb serotonin. However, this hypothesis requires further verification, since factor XIII also changes the serotonin concentration in the tissues of irradiated animals.

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