

ROLE OF THE LIVER IN THE MECHANISM FOR REDUCING THE BLOOD SEROTONIN CONCENTRATION IN ACUTE RADIATION SICKNESS

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Experiments on rabbits irradiated in a dose of 600 R (Co^{60} γ rays, 120 R/min) showed that at the height of acute radiation sickness the supply of serotonin from the enterochromaffin cells into the blood stream is undisturbed. In irradiated animals much of the serotonin contained in blood draining from the intestine is broken down in the liver, which is not observed in intact animals. At the height of acute radiation sickness monoamine oxidase activity in the liver rises sharply.

The blood serotonin concentration falls in acute radiation sickness [3, 4]. It is considered that this phenomenon is based on a disturbance of the synthesis and secretion of serotonin in the enterochromaffin cells of the gastro-intestinal tract [4]. However, this hypothesis is contradicted by results showing the relative radioresistance of the Kulchitsky cells [2] and the absence of sharp changes in the serotonin content in the intestine at the height of acute radiation sickness [6]. After irradiation the content of 5-hydroxy-indole-acetic acid excreted in the urine is increased [5, 6], evidence of more rapid serotonin metabolism. However, the data on activity of monoamine oxidase, the key enzyme in the chain of biological inactivation of serotonin in acute radiation sickness, are highly contradictory [1, 4, 10].

The object of the present investigation was to study the supply of serotonin from the intestine into the blood stream and its breakdown in the liver in acute radiation sickness.

EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on 30 chinchilla rabbits weighing 2.1-2.6 kg, of which 15 animals were exposed to a single dose (600 R, 120 R/min) of whole-body irradiation with Co^{60} γ rays. Under pentobarbital anesthesia blood was obtained from the portal vein and inferior vena cava (at the point where it receives the hepatic vein) in 11 healthy and 11 irradiated rabbits (on the 7th day after irradiation). The serotonin concentration in the samples of blood thus obtained was determined by the spectrofluorometric method of Weissbach [11]. Monoamine oxidase activity was determined in 3 healthy and 5 irradiated animals by the histochemical method of Glenner et al. [8].

The serotonin concentration in blood from the portal vein of the irradiated animals was indistinguishable ($P > 0.05$) from that in the healthy animals (Table 1). This suggests that the supply of serotonin from the enterochromaffin cells into the blood stream was undisturbed at the height of acute radiation sickness.

The serotonin concentration in blood from the inferior vena cava of the healthy animals showed a very slight decrease compared with its concentration in blood from the portal vein. In the irradiated animals, on the other hand, the serotonin level in blood from the inferior vena cava was reduced by almost half compared with that in blood from the portal vein (Table 1). These results suggest that at the height of acute radiation sickness much of the serotonin reaching the blood from the intestine is broken down in the liver.

Research Institute of Medical Radiology, Academy of Medical Sciences of the USSR, Obninsk. (Presented by Academician of the Academy of Medical Sciences of the USSR G. A. Zedgenidze.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 75, No. 1, pp. 33-34, January, 1973. Original article submitted October 1, 1971.

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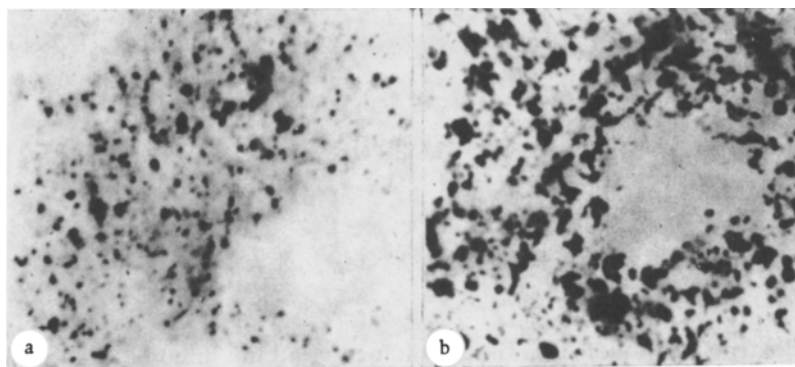


Fig. 1. Monoamine oxidase activity in liver of healthy (a) and irradiated (b) rabbits. A sharp increase is observed in the number and size of the formazan granules in the liver of the irradiated rabbit (720x).

TABLE 1. Blood Serotonin Concentration (in $\mu\text{g/ml}$) and Monoamine Oxidase Activity (in conventional units) in Liver of Healthy and Irradiated Rabbits ($M \pm m$)

Animals	Blood serotonin concentration		Liver monoamine oxidase activity
	portal vein	inferior vena cava	
Healthy	1.30 ± 0.06	1.08 ± 0.09	2
Irradiated	1.19 ± 0.17	0.65 ± 0.11	6

As will be clear from Table 1 and Fig. 1, monoamine oxidase activity in the liver rose sharply in the irradiated animals. These results are further evidence of an increase in the intensity of serotonin breakdown in the liver at the height of acute radiation sickness.

Most of the blood serotonin in intact animals is known to be contained in the platelets. In acute radiation sickness, when thrombocytopenia develops and the platelets are less able to absorb serotonin [4], since the supply of serotonin from the enterochromaffin cells into the blood stream remains adequate the concentration of "free" serotonin in the plasma must evidently rise. This presumably leads to a compensatory increase in the activity of monoamine oxidase, which metabolizes serotonin to 5-hydroxyindole-acetic acid. The possibility cannot be ruled out that the increase in monoamine oxidase activity during irradiation is due to liberation of the enzyme from damaged mitochondria, where this enzyme is found in the matrix.

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