CHANGES IN THE BLOOD SEROTONIN CONCENTRATION AND THE CONTENT OF 5-HT-ORGANELLES IN RABBIT PLATELETS IN ACUTE RADIATION SICKNESS

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The decrease in the blood serotonin concentration of rabbits with acute radiation sickness is due, not only to a decrease in the platelet count, but also to a decrease in the number of serotonin-containing granules in the platelets themselves.

Serotonin (5-HT) is contained in the blood mainly in the platelets [6]. A decrease in the serotonin concentration in the blood in radiation sickness has therefore been explained by the decrease in the platelet count [2, 3]. Some investigators have noted that the serotoninopenia occurs sooner during the development of acute radiation sickness, and is more marked in degree than the thrombocytopenia [1, 5]. In their opinion, this may indicate a change in the concentration of serotonin in the platelets themselves. However, no special analysis has yet been made of the serotonin content in the platelets after irradiation.

It is now generally accepted that serotonin is located in 5-HT-organelles: spherical electron-dense granules measuring 500-2000 Å, detected in platelets fixed in glutaraldehyde [7]. Since these granules are easily identified morphologically, an attempt was made to study the serotonin content in the platelets in various stages of acute radiation sickness in rabbits by counting these granules.

EXPERIMENTAL METHOD

Experiments were carried out on 20 chinchilla rabbits of both sexes weighing from 2 to 2.9 kg. A single exposure to whole-body irradiation by Co^{60} γ-rays was given in a dose of 600 R (dose rate 140 R/min). Before and at different times after irradiation (1, 4, 7, 10, 15, and 21 days) 5-10 ml blood was taken from the animals' heart with a silicone-treated needle. Serotonin concentration was determined spectrofluorometrically [8]. The platelet count was determined in blood by Fonio's method.

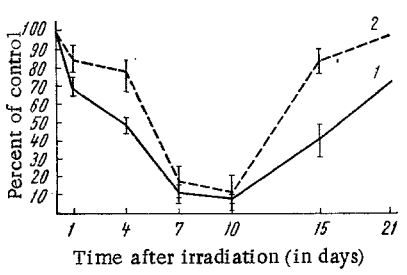

Fig. 1. Serotonin concentration (1) and platelet count (2) in blood of rabbits in various stages of acute radiation sickness.

For the electron-microscopic analysis the platelets were isolated by centrifuging the blood twice at 90 g for 10 min and the supernatant plasma at 700 g for 7 min. The residue, consisting of platelets, was fixed in Karnovsky's fluid and additionally in Palade's solution, dehydrated in alcohols of increasing concentration, and embedded in Araldite. Sections were cut on the LKB-4800 A ultratome, shadow-cast with lead citrate by Reynolds' method, and examined in the JEM-5y electron microscope. The number of 5-HT-organelles was counted in 600-900 sections, and the number of sections containing 0, 1, 2, 3, 4, 5, and 6 serotonin granules was determined.

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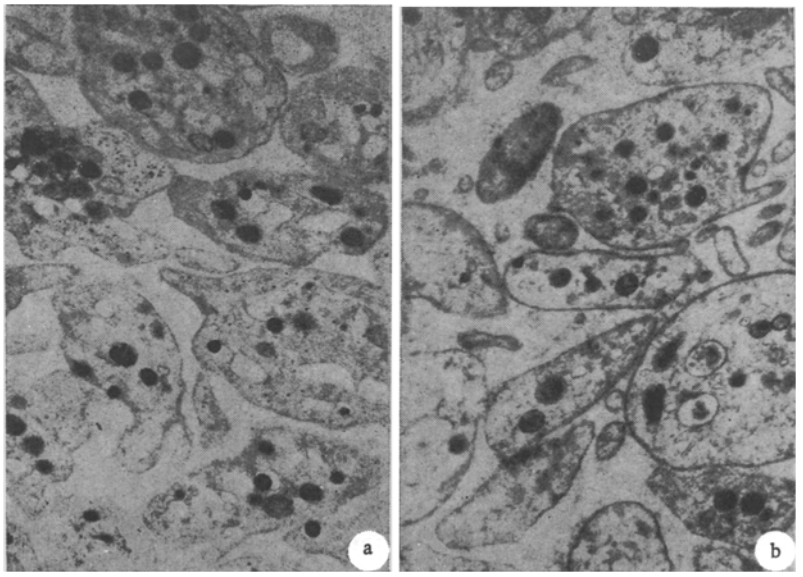

Fig. 2. Ultrastructure of platelets (17,400 ×): A) platelets of an unirradiated rabbit; B) platelets of an irradiated rabbit (7th day after irradiation). 1) 5-HT-organelles; 2) α-granules; 3) mitochondria.

EXPERIMENTAL RESULTS

The serotonin concentration in the blood of the unirradiated animals was 2.35 ± 0.56 μg/ml ($M \pm \sigma$) and the platelet count was $653{,}000 \pm 159{,}000/mm^3$ blood. On the 1st day after irradiation the serotonin concentration was reduced by 35%, and on the 4th day by 50% (Fig. 1). At the height of the radiation sickness (7th and 10th days) the serotonin concentration was reduced by more than 10 times below the control level. On the 15th day slight recovery of the serotonin concentration was observed, and by the 21st day the blood serotonin level was 66% of the control.

The thrombocytopenia was not so marked as the serotoninopenia in the various stages after irradiation. On the 1st and 4th days after irradiation the platelet count still did not differ significantly from the control. At the height of radiation sickness (the 7th and 10th days) the platelet count showed a sharp decrease, by the 15th day it had started to rise again, and by the 21st day it reached the control level.

Changes in the blood serotonin concentration in the various periods of acute radiation sickness were not always parallel to the decrease in the platelet count. In the early stages after irradiation (1st and 4th days) the serotoninopenia was more marked than the thrombocytopenia. Restoration of the serotonin concentration took place more slowly than restoration of the normal platelet count. This phenomenon may be explained by a decrease in the serotonin concentration in the platelets themselves. This was confirmed by investigations of the number of 5-HT-organelles in the platelets (Fig. 2).

On the 1st day after irradiation the number of serotonin granules per hundred sections of platelets was unchanged compared with its initial value (148 ± 15.1 and 149 ± 4.8, respectively), but on the 4th day their number showed a significant ($P < 0.05$) decrease (133 ± 4.1). At the height of the disease (7th day) the number of granules was reduced by 35% (110 ± 4.7; $P < 0.05$), on the 15th day it had started to increase (141 ± 16.3), and by the 21st day it was back to its original level (152 ± 4.8).

The study of the distribution of 5-HT-organelles in the platelets at various times after irradiation yielded evidence of qualitative changes in the platelets.

As Fig. 3 shows, in the postradiation period the population of platelets not containing granules was increased, while the number of platelets with 2, 3, and 4 granules was reduced. This phenomenon was particularly marked at the height of radiation sickness. On the 21st day the distribution of 5-HT-organelles was not significantly different from the control.

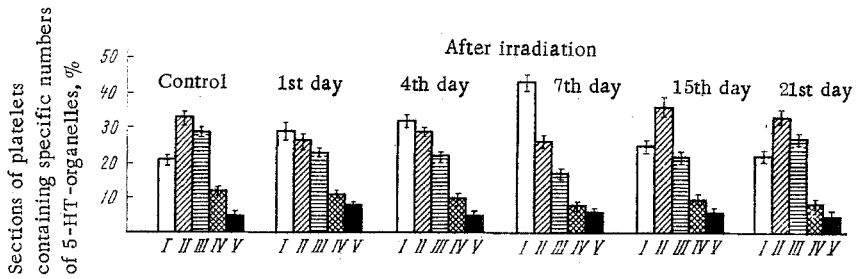

Fig. 3. Distribution of 5-HT-organelles in rabbit platelets at different stages of acute radiation sickness: I) without 5-HT-organelles; II) with 1; III) with 2; IV) with 3; V) with 5 5-HT-organelles.

The serotoninopenia arising in rabbits during acute radiation sickness is thus due not only to a decrease in the number of platelets, but also to a decrease in the concentration of serotonin in the platelets themselves. This is shown indirectly by the more marked decrease in the blood serotonin level compared with the thrombocytopenia in the early stages after irradiation (the first and 4th days) and also by the slower recovery of the serotonin concentration than of the platelet count in the blood. A decrease in the level of this compound in the platelets is also shown by the results of counting the 5-HT-organelles. Not only a decrease in the number of serotonin granules in the various periods of acute radiation sickness, but also qualitative changes in the platelets relative to their content of 5-HT organelles were detected. The decrease in the serotonin concentration in the platelets after irradiation is evidently due to an increase in the number of platelets with a lower content of this amine.

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