

THE EFFECT OF ANTIBIOTIC THERAPY ON THE SEROTONIN  
AND HISTAMINE CONTENT IN THE BLOOD AND ORGANS  
OF IRRADIATED RABBITS

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A great deal of attention is given in numerous communications to the role of serotonin (5-oxytryptamine, abbreviated 5-OTA) and histamine in the pathogenesis of radiation disease. A marked decrease in 5-OTA has been established in the blood and organs of irradiated animals [5, 6, 11]. There are data on changes in the histamine content and the inhibition of histaminase activity in the blood and organs on irradiation [1, 7, 8, 16]. Administration of 5-OTA and its precursors as well as histamine has a protective action in radiation disease [2, 13, 20]. Moreover, a number of studies indicate various quantitative changes in 5-OTA and histamine in the blood, organs and cells of normal animals [9, 15, 17, 18, 21] and a lesser decrease in the 5-OTA level in the blood of irradiated animals effected by antibiotics.

We were interested in tracing the dynamics of quantitative variations of 5-OTA and histamine in the blood and organs of irradiated and nonirradiated rabbits on prolonged administration of antibiotics.

#### EXPERIMENTAL METHODS

Experiments were conducted on 96 male rabbits weighing  $2\frac{1}{2}$ –3 kg each. Each experiment was conducted on 24 animals. Altogether there were 4 experiments. The animals were divided into 4 equal groups: 1) irradiated, 2) irradiated and treated with antibiotics, 3) nonirradiated treated with antibiotics, 4) nonirradiated and administered physiological solution. The rabbits of the 1st and 2nd group were subjected to a single x-ray dosage of 950 r. Antibiotics were administered 12–15 h after irradiation. Penicillin and streptomycin were administered intramuscularly (in doses of 100,000 units), levomycetin – orally (in doses of 100 mg) twice daily for a period of 3 weeks.

The quantities of 5-OTA and histamine in rabbits' blood of all groups were determined in the normal state and subsequently in the blood and organs 1, 3, 7, 10, 14 and 21 days after irradiation. Two ml of blood and 1 g of each organ homogenate were used to determine the level of 5-OTA and histamine. The 5-OTA from the blood and organs was extracted by acetone (10 ml per ml of blood and 20 ml per g of organ homogenate) for a period of 2 days at 4–5°, the histamine by a 10% (weight/volume) solution of trichloroacetic acid (2 ml per ml blood and 7 ml per g of organ homogenate) during 24 h at the same temperature. Acetone was removed under vacuum at 45°. The dry residue was dissolved in Gaddum fluid.

Quantitative determination of 5-OTA was conducted on an isolated atropinized rat's colon [10]; histamine – on an isolated atropinized guinea pig ileum at 37°. The results were examined statistically.

#### EXPERIMENTAL RESULTS

Irradiation markedly diminished the quantities of 5-OTA and histamine in the animals' blood. In rabbits of the 1st group the amount of 5-OTA [0.122 mg/ml (0–0.244)] was decreased approximately to  $\frac{1}{10}$  and that of histamine [(0.102 mg/ml) (0.019–0.195)] to  $\frac{1}{8}$  in 14 h after irradiation as compared to the corresponding 5-OTA level

[1.2 mg/ml (0.98-1.42)] and of histamine [0.83 mg/ml (0.61-1.05)] in the blood before irradiation. The amount of 5-OTA remained  $\frac{1}{5}$  to  $\frac{1}{12}$  and of histamine  $\frac{1}{10}$  to  $\frac{1}{40}$  of the initial level in the subsequent 20 days of observation.

Treatment of irradiated rabbits by antibiotics produced no effect on the marked decrease of 5-OTA and brought about a statistically unreliable decrease in the fall of the histamine level in the blood. Administration of antibiotics to nonirradiated rabbits caused a fairly rapid and regular decrease in the quantity of 5-OTA (on the average to  $\frac{1}{3}$  -  $\frac{1}{10}$ ) and histamine (on the average to  $\frac{1}{3}$  -  $\frac{1}{16}$ ) in the blood as compared with the initial magnitude.

The rabbit's brain responded to irradiation and antibiotic administration by definite quantitative variations of 5-OTA and histamine.

In animals of the 1st group the amount of 5-OTA in the brain [0.248 mg/g (0-0.496)] was on the average  $\frac{1}{16}$  of the control [4.02 mg/g (1.17-6.87)] during the first 7 days after irradiation. Ten days after irradiation the level of 5-OTA in the brain returned to normal and subsequently remained the same. The histamine quantity [0.039 mg/g (0.17-0.061)] in the rabbit's brain of the 1st group decreased approximately to  $\frac{1}{70}$  24 h after irradiation and remained  $\frac{1}{27}$  -  $\frac{1}{65}$  of the corresponding magnitude [2.7 mg/g (1.23-4.17)] of nonirradiated animals in the subsequent periods of observation.

Administration of antibiotics to irradiated rabbits inhibited restoration of 5-OTA to normal levels and exhibited no clear effect on quantitative variations of histamine in the brain caused by irradiation. During 14 days the magnitude of 5-OTA in the rabbit's brain of the 2nd group was  $\frac{1}{10}$  -  $\frac{1}{32}$  and after 21 days  $\frac{1}{4}$  of the corresponding magnitudes of that in intact animals. The histamine level in the brain of rabbits of the 2nd group was on the average  $\frac{1}{30}$  -  $\frac{1}{60}$  of that of the nonirradiated animals. Administration of antibiotics decreased the 5-OTA and histamine in the brain of nonirradiated animals. In rabbits of the 3rd group the 5-OTA content [0.219 mg/g (0.03-0.048)] was on the average  $\frac{1}{18}$  of the norm, while the histamine level was close to the corresponding indices of the rabbits of the 1st and 2nd groups.

Irradiation caused a considerable decrease in the amount of 5-OTA and histamine in the rabbits' small intestine. In 24 h after irradiation the quantity of 5-OTA and histamine [0.116 mg/g (0.103-0.129)] in the small intestines of rabbits of the 1st group decreased to  $\frac{1}{60}$  or less, that of histamine to  $\frac{1}{20}$  by comparison with the corresponding magnitudes of nonirradiated rabbits [5-OTA - 7.24 mg/g (3.7-10.78) and 2 mg/g (1.05-2.95)]. At subsequent periods after irradiation the 5-OTA content of the rabbits' small intestines of the 1st group gradually increased, but still remained 7.2-13 times lower than the content in intact rabbits; the histamine level [0.037 mg/g (0.015-0.059)] decreased even more and was  $\frac{1}{50}$  -  $\frac{1}{60}$  of the level in control animals. Administration of antibiotics to irradiated rabbits, it would seem, lessened the marked decline of 5-OTA and histamine levels in the small intestine caused by irradiation. However, statistical treatment of results indicated the uncertainty of this effect. A protracted administration of antibiotics to nonirradiated rabbits did not materially change the quantity of 5-OTA and considerably decreased the histamine content in the small intestine. The histamine level in the small intestines of the 3rd rabbit group decreased soon after the beginning of antibiotic administration and remained  $\frac{1}{7}$  -  $\frac{1}{25}$  of the corresponding control indices.

Administration of physiologic solution to nonirradiated rabbits produced no effect on the levels of 5-OTA and histamine in their blood and small intestine and produced statistically authentic decreases in the amount of 5-OTA in the brain after 10, 14, 21 days and histamine after 14 days.

Thus, a single total x-ray irradiation (950 r) of rabbits caused a marked decrease in the amount of 5-OTA and histamine in the blood, brain, small intestine which is related to a decrease in the quantity of blood thrombocytes as well as the disruption of the enzymatic systems partaking in the formation and metabolism of these biogenic amines [1, 8, 16]. A protracted administration of antibiotics did not impede the level variations of 5-OTA and histamine in the blood and organs of rabbits in conditions of irradiation. Some decrease in the fall of the 5-OTA level in the small intestines of irradiated rabbits treated by antibiotics may be related to the sterilization of the intestines and prevention of bacterial metabolism of dietetic tryptophan and the pharmacological activity of antibiotics [17, 18]. The decrease of 5-OTA and histamine content in the blood and organs of nonirradiated rabbits on protracted administration of antibiotics may be explained as the stimulatory action of antibiotics on the hypophysis system - suprarenal body, which produces hormone secretion [3-4] exerting an influence on the level of 5-OTA, histamine and on their metabolism [12, 14, 19] as well as the direct effect of antibiotics on the metabolism of 5-OTA and histamine.

## SUMMARY

Single total x-ray irradiation of rabbits (in a dose of 950 r) caused considerable reduction of serotonin (5-hydro-tryptamine) and of histamine level in the blood, brain and small intestine. Three-week antibiotic treatment of the irradiated rabbits had no significant effect on the marked reduction of serotonin content in the blood, brain, and of histamine in the blood, brain and small intestine; it also failed to materially affect the serotonin content in the small intestine.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

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