SPECIFICITY OF NUCLEOSIDURIA IN THE IRRADIATED ANIMAL

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After γ-ray irradiation, immunization, administration of cortisone, and burns the excretion of thymidine in the urine of rats increases. Irradiation produces the greatest increase in excretion. The action of these factors leads to an approximately equal increase in excretion of β-aminoisobutyric acids in the urine.

The postradiation increase in excretion of desoxynucleosides (desoxycytidine and thymidine) in the urine of animals and man can be used as an early diagnostic test of radiation damage. Among the metabolic tests of radiation damage in animals (rats), nucleosiduria is the most radiosensitive index, with precise dependence on dosage and with a high relative rate of increase [1, 2, 6, 7, 9, 10, 13-15, 17].

However, it has not yet been discovered to what extent nucleosiduria is specific for the irradiated organism. Parisek and co-workers [7] did not observe an increase in the excretion of desoxycytidine in the urine of rats during the first day after several types of treatment accompanied by massive death of cells (extensive third degree burns, multiple fractures of both limbs, necrotic inflammatory changes after injection of formalin into the animal's foot). Yakubovic and co-workers [18] found a definite increase in the concentration of desoxycytidine in the urine during the first day after injection of hydrocortisone into rats, causing disintegration of lymphocytes.

The object of the present investigation was to study the excretion of thymidine and its breakdown product β-aminoisobutyric acid (BAIBA) in rats after exposure to various factors causing destruction of tissue cells: γ-ray irradiation (CO^{60}), severe third degree burns, immunization, and administration of hydrocortisone.

Increased excretion of BAIBA in the urine is nonspecific for the irradiated animal and also takes place in a number of diseases accompanied by cell destruction [6, 11, 16]. During exposure to the above-mentioned pathogenetic factors, it was therefore decided to compare the levels of excretion of thymidine and BAIBA in the urine.

METHOD AND RESULTS

Experiments were carried out on 120 noninbred male rats weighing 170-200 g, which were kept in metabolism cages on an ordinary diet.

The animals (20) of group 1 received whole-body γ-ray irradiation in a dose of 500 R on an ÉGO-2 apparatus (dose rate 640 R/min). The animals (40) of group 2 were immunized by intramuscular injection of heat-killed vaccine of Salmonella paratyphosa Breslau (1 billion bacterial cells in 0.5 ml solution). Third degree burns were inflicted on the 40 animals of group 3. The burned areas in the lumbosacral region covered 10-15% of the animal's body surface. The 20 animals of group 4 received an intraperitoneal injection of hydrocortisone in a dose of 5 mg/100 g body weight (1.3-1.6 ml of the preparation manufactured by Gedeon Richter, Hungary).

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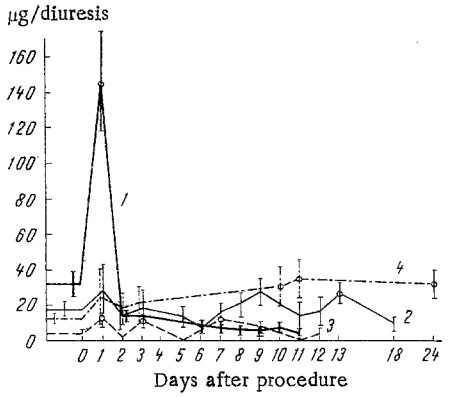

Fig. 1. Dynamics of excretion of thymidine in urine of rats after various procedures: 1) irradiation; 2) immunization; 3) hydrocortisone; 4) burns. Circles denote values differing significantly from original level. Vertical lines on curves show biological scatter of values.

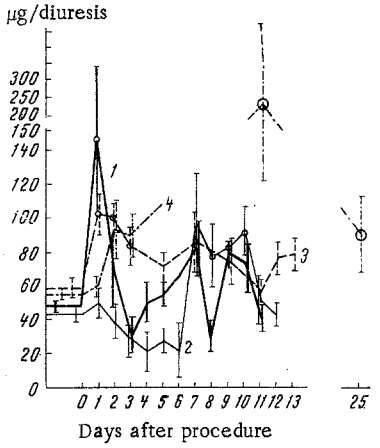

Fig. 2. Dynamics of excretion of BAIBA in urine of rats after various procedures. Legend as in Fig. 1.

Thymidine was determined by Mazurik's method [5], BAIBA by Bowden's method [12] (in a modification using the Soviet KU-1 ion-exchange resin, chromatography of amino-acid extracts on paper was carried out in a system of normal butanol–formic acid–water in the ratio 75 :15 :10). Thymidine and BAIBA in the 24-h urine of the animals were determined for 11-25 days after each procedure. The results obtained were subjected to statistical analysis by Student's method.

Data for excretion of thymidine in the urine of rats during the 24 h after irradiation, injection of cortisone, burns, and immunization are shown in Fig. 1. After irradiation of the animals, the excretion of thymidine reached a maximum during the first day, when it was 5-6 times above the background level, and later after irradiation its content in the 24-h urine was below the control value. After injection of hydrocortisone, a significant increase in thymidine excretion was found on the first, third, and seventh days (by 3-4 times), on the 10th, 11th, and 24th days after third degree burns (by 2.6 times), but only on the 13th day after injection of vaccine to produce immunization of the animals (by 1.5 times).

Data for the excretion of BAIBA in the urine during the 24 h after these procedures are given in Fig. 2. After irradiation of the animals, excretion of BAIBA with the urine reached a maximum during the first day, when it was 2.5-3 times above the background value; later, after irradiation, changes in the BAIBA content in the 24-h urine were not statistically significant. After burns, a significant increase in the excretion of BAIBA in the urine occurred on the second, third, 11th, and 25th days (on the average by 2.5 times), after immunization of the animals on the seventh, eighth, ninth, and 10th days after injection of vaccine (on the average by 2.5 times), and after injection of hydrocortisone on the first, second, third, and seventh days (on the average by 1.5 times).

All the pathogenetic factors tested thus increased the excretion of thymidine and BAIBA in the rats' urine. However, the degree and times of increase in thymidine excretion differed after each of the four types of procedure. As regards the degree of increase in thymidine excretion, the first place goes to irradiation, followed (in descending order) by injection of hydrocortisone, burns, and immunization. By contrast with excretion of thymidine in the urine, the degree of increase of BAIBA excretion after three types of procedure (irradiation, burns, immunization) was approximately equal, and it was somewhat less only after injection of hydrocortisone. On the first day after these various procedures, a statistically significant increase in the excretion of thymidine and BAIBA in the urine took place only after irradiation and injection of hydrocortisone, and it was most marked after irradiation. After irradiation of the rats the increase in excretion of thymidine in the urine was twice as great as the increase in excretion of BAIBA in the urine.

The increase in excretion of BAIBA and thymidine between the first and seventh days after injection of hydrocortisone and the increase in excretion of BAIBA on the second and third days after burns can be attributed to breakdown of cells in the damaged tissues. The increases in content of BAIBA and thymidine in the urine in the later periods after burns (on the 10th-25th days) coincides with the beginning of processes of tissue repair [4]. The increase in excretion of BAIBA from the seventh to the 11th days and of thymidine on the 13th day after immunization of the animals was probably the result of death of some plasma cells preceding the liberation of antibodies into the blood stream [3, 7].

The results of these experiments show that thymidinuria may be due to two principal causes: 1) multiple destruction of tissue cells (especially lymphocytes) by the pathogenetic factors used at different times after the beginning of the procedure, and 2) by the processes of tissue repair, accompanied by an increase in the quantity of DNA precursors formed de novo. However, since selective destruction of cells of rapidly renewed tissues and of lymphoid tissue in the earliest stages after exposure to the procedure is one of the "critical" effects of ionizing radiation, the determination of an increase in the content of desoxynucleosides and, in particular, of thymidine in the urine can be used as a highly sensitive indicator of radiation damage.

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