EFFECT OF IONIZING RADIATION ON THE URIC ACID AND ALLANTOIN CONTENTS OF THE BLOOD AND URINE OF ANIMALS

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The object of the present reseach was to investigate the effects of lethal doses of γ- and α-radiation on the contents in the blood and urine of different species of animals of the end-products of nucleic acid metabolism – uric acid and allantoin.

EXPERIMENTAL METHODS

Our experiments were performed on 12 dogs and 8 rats.

Male dogs weighing from 24 to 30 kg were maintained on a strictly regulated diet. Blood uric acid was determined by the method of Caraway [3], and blood allantoin by that of Young, MacPherson and Conway [5, 6].

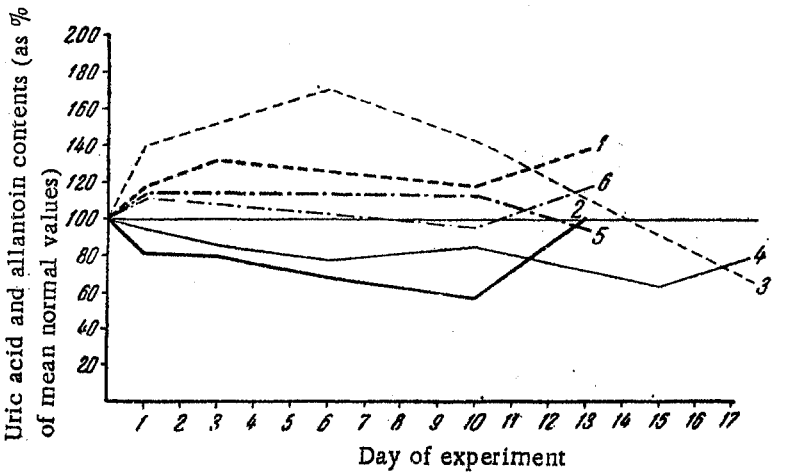

Fig. 1. Blood uric acid and allantoin contents of dogs after exposure to γ-ray dosages of 350 and 400 r.
Allantoin (1) and uric acid (2) after exposure to 400 r of radiation; allantoin (3) and uric acid (4) after exposure to 350 r of radiation; allantoin (5) and uric acid (6) in control animals.

The analysis were performed 5-6 times, at 2-5 day intervals, for each dog before it was exposed to irradiation.

The first group consisted of 4 dogs, which were subjected to total γ-ray irradiation in single doese of 350 r (2 dogs) and 400 r (2 dogs). Blood samples (7 ml) were taken for analysis from the femoral vein and artery. The

TABLE 1

Uric Acid and Allantoin Contents of Blood from the Portal and Hepatic Veins, and from the Arterial System of Normal Dogs

Name of dog	Uric acid						Allantoin					
	in arterial blood	in portal vein blood	secreted from the intestinal wall (+)	in the blood flowing to the liver	in hepatic vein blood	removed by the liver (−)	in arterial blood	in portal vein blood	secreted from the intestinal wall (+)	in the blood flowing to the liver	in hepatic vein blood	removed by the liver (−)
	mg-%	mg-%	%	mg-%	mg-%	%	mg-%	mg-%	%	mg-%	mg-%	%
Dozor	0,57	0,68	+19,3	0,64	0,51	—20,3	3,35	3,58	+ 6,9	3,49	3,11	—10,9
Volchok	0,51	0,75	+47,0	0,67	0,54	—19,3	3,33	3,50	+ 5,1	3,44	2,90	—15,4
Migai	0,44	0,56	+27,3	0,52	0,48	— 7,7	2,68	2,98	+11,2	2,86	2,65	— 7,4
Mean . . .	0,51	0,66	+29,4	0,61	0,51	—16,4	3,12	3,35	+7,7	3,26	2,89	—11,5

TABLE 2

Uric Acid and Allantoin Contents of Blood from the Portal and Hepatic Veins and from the Arterial System of a Control Dog and of Dogs Following Irradiation

Condition of animal	Uric acid						Allantoin					
	in arterial blood	in portal vein blood	secreted by the intestinal wall (+)	in the blood flowing to the liver	in hepatic vein blood	removed by the liver (−)	in arterial blood	in portal vein blood	secreted by the intestinal wall (+)	in the blood flowing to the liver	in hepatic vein blood	removed by the liver (−)
	mg-%	mg-%	%	mg-%	mg-%	%	mg-%	mg-%	%	mg-%	mg-%	%
Normal values for the control dogs	0,44	0,56	+27,3	0,52	0,48	— 7,7	2,68	2,98	+11,2	2,88	2,65	— 7,4
1st day of experiment	0,43	0,57	+32,6	0,52	0,47	— 9,6	3,32	3,78	+13,9	3,67	3,14	—13,5
2nd " " "	0,43	0,53	+23,3	0,50	0,48	— 4,0	2,86	2,96	+ 3,5	2,93	2,80	— 4,4
3rd " " "	—	—	—	—	—	—	2,36	2,52	+ 6,8	2,47	2,24	— 9,3
7th " " "	0,39	0,58	+48,7	0,52	0,55	+ 5,8	2,80	3,42	+22,4	3,21	3,14	— 2,2
10th " " "												
Normal value (mean) for 3 dogs	0,51	0,66	+29,4	0,61	0,51	—16,4	3,12	3,35	+ 7,7	3,26	2,89	—11,5
After irradiation:												
1st day	0,55	0,76	+38,2	0,69	0,42	—39,1	3,02	3,72	+23,2	3,49	3,23	— 7,5
3rd "	0,50	0,60	+20,0	0,57	0,32	—43,9	3,08	3,50	+13,6	3,36	3,12	— 7,1
7th "	0,39	0,58	+48,7	0,52	0,32	—38,5	3,29	3,73	+13,4	3,58	3,45	— 3,6
10th "	0,38	0,55	+44,7	0,49	0,30	—38,8	3,47	3,64	+ 4,9	3,58	3,14	—12,0

second group consisted of 3 dogs, on which an angiostomy had been performed by E. S. London's procedure [1], with application of skin cannulae (by I. A. Pigalev's procedure [2]) to the portal and hepatic veins; these dogs were exposed to a single γ-ray irradiation of the whole body, at a dosage of 400 r. Blood samples were taken from the portal and hepatic veins and from the femoral artery. Since in unit time 2/3 of the blood supply of the liver enters via the portal vein, and 1/3 via the hepatic artery (E. S. London), the overall average concentration of uric acid and allantoin in the blood entering the liver can hence be calculated.

Irradiation was performed using an EGO-2 equipment, delivering a dose of 506-538 r/min., with an exposure time of 40.6-47.4 seconds. The animals died on the 14-17th day after irradiation.

The third group consisted of two dogs, which were treated with polonium (doses of 0.06 mC/kg, administered subcutaneously). The animals died on the 28th and 30th day after the injections.

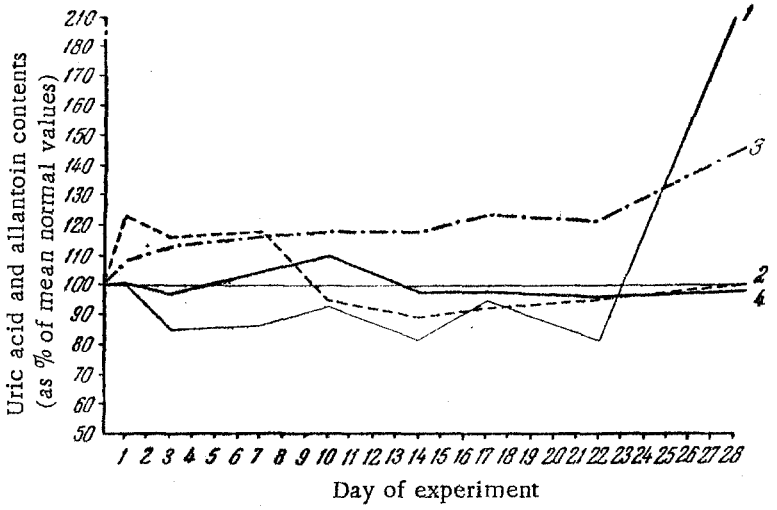

Fig. 2. Mean uric acid and allantoin contents of the blood of two dogs after administration of polonium (at dosage of 0.06 mC/kg), and of a control dog.
Uric acid in polonium-treated dogs (1) and in the control dog (2); allantoin in polonium-treated dogs (3) and in the control dog (4).

Blood samples were taken for analysis at 2-5-day intervals during the course of radiation sickness.

Parallel with each group of experimental animals we analyzed blood samples from a control dog, which was maintained on the same daily food ration as was consumed by one of the irradiated dogs.

Male rats, weighing 180-200 g, were kept in metabolism cages on a standard diet consisting of pellets containing 60% of starch, 20% of casein, 10% of animal fat, 3% of yeast and 5% of salt mixture. Uric acid was determined in the 24-hour urine output, by Borsook's method [4], and allantoin by Young and Conway's method [5]. We analyzed 6-8 24-hour portions of urine from each rat before exposing the animals to irradiation. Four of the eight rats were then given subcutaneous injections of polonium (dosage level 0.1 mC/kg). The animals survived for from 5 to 12 days. The remaining 4 rats served as control animals. They were given the same daily ration as was consumed by the injected rats. The urine of the polonium-treated rats was analyzed daily, beginning with the first day after injection.

EXPERIMENTAL RESULTS

The uric acid contents of arterial and venous blood taken from the dogs of the first group were practically identical before irradiation. The values for arterial blood were 0.54 ± 0.041 to 0.75 ± 0.041 mg %*, giving a

* In the statistical treatment of the numerical data the standard deviation m was derived from the formula $m = \pm \frac{\sigma}{\sqrt{N}}$, where σ is the mean square error, and N is the number of determinations.

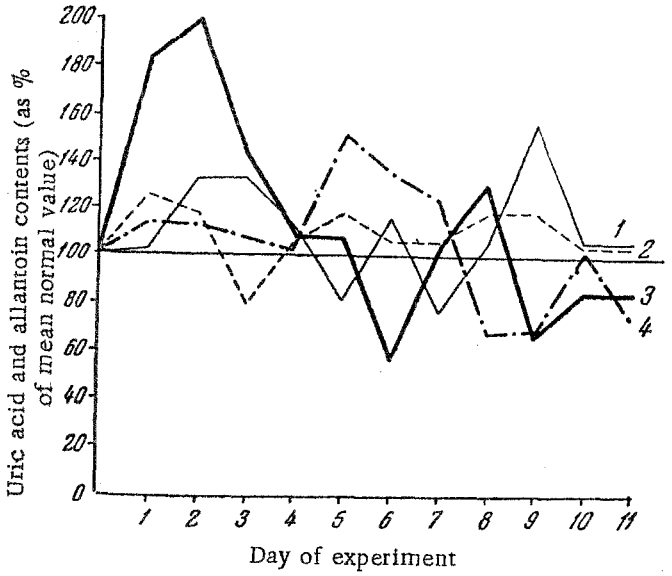

Fig. 3. Mean uric acid and allantoin contents of 24-hour portions of urine from four rats, after administration of polonium (at dosage of 0.1 mC/ kg), and from four control rats (as percentages of the mean normal value).
Allantoin from polonium-treated rats (1) and from the control rats (2); uric acid from polonium-treated rats (3) and from control rats (4).

mean value of 0.62 mg-%. The allantoin content was practically identical for venous and arterial blood, and varied for arterial blood within the range 2.65 ± 0.09 to 3.23 ± 0.088 mg %, giving a mean value of 2.8 mg %.

It may be seen from Fig. 1 that the blood uric acid content varied within the normal range for the control animals, with a tendency toward higher values, while the allantoin content rose by 12-14%. The uric acid content of the serum of irradiated dogs fell by 20-30%, on the average, and serum allantoin rose by 25-40%.

The results given by the second group of dogs related to uric acid and allantoin metabolism in the liver and intestinal wall.

It is evident from the data of Table 1 that under normal conditions the highest contents of uric acid and allantoin were found in the blood from the portal vein, as compared with that of the hepatic vein and of the arterial system.

It may be supposed that the processes of synthesis of uric acid and formation of allantoin take place chiefly in the walls of the small intestine. That these substances are not of exogenous origin is shown by the results of special experiments in which the dogs were fasted for 4 days. Under such conditions, which completely excluded the possibility that uric acid and allantoin could have been derived from ingested food, both of these substances continued to be secreted into the blood stream from the intestine.

In normal animals the liver removes uric acid from the blood passing through it (from 6 to 20%), as well as allantoin (from 7 to 16%).

Table 2 shows the corresponding mean results obtained from the same dogs after irradiation and from the control dog. The uric acid content of blood taken from the specified vessels of the control angiostomized dog receiving a restricted food ration during the experiment did not vary beyond the limits of the normal range for this dog. It was not until the 10th day, when the dog showed clear signs of undernourishment, that the uric acid content of hepatic vein blood rose slightly, and that its retention by the liver ceased to be evident. The allantoin content of all the blood samples was high on the 1st and the 10th day of the experiment, and its retention by the liver was smaller on the 3rd and the 10th day.

Apart from the first few days after irradiation with γ-rays, there was a regular decline in the uric acid content of the blood from the various vessels, to a minimum on the 7-10th day. In comparison with the initial mean normal values, the uric acid content of blood from the portal vein fell by 16.7%, of arterial blood by 25.5%, and of hepatic vein blood by 41.2%. The allantoin content was in general raised (except in the case of arterial blood on the 1st and the 3rd days after irradiation).

The amount of uric acid removed from the blood by the liver was 2½ times greater than in normal animals. The amount of allantoin removed by the liver had fallen to a third of the normal amount on the 7th day after irradiation.

The increase in the amount of uric acid removed by the liver, considered in conjunction with the rise in allantoin in hepatic vein blood, indicates that oxidation of uric acid to allantoin in the liver is intensified in irradiated animals.

Production of uric acid in the wall of the small intestine rose slightly as the course of radiation sickness progressed (roughly as for the control dog, on the 10th day), as is shown by the rise in uric acid content of portal vein blood. Formation of allantoin in the walls of the small intestine of irradiated dogs also rose as the disease progressed (except on the 10th day), whereas in the control dog there was no increase in allantoin from this source until the 10th day.

Fig. 2 shows the mean value found for two dogs treated with polonium (third group), with the corresponding results for the control dog. The uric acid content of the arterial blood of these dogs varied, before the injections, within the range 0.54 ± 0.063 to 0.61 ± 0.012, mean value 0.64 mg %; the allantoin content varied from 2.65 ± 0.023 to 3.21 ± 0.144 mg %, mean value 2.95 mg %. The blood uric acid of these dogs fell by 15% from the 3rd day after injection of polonium, and remained at a low level until the death of the animals. The allantoin content rose from the second day after administration of polonium, being 29% above the normal on the 17th day, and 40% above normal at death. The uric acid content found for the undernourished control dog rose, on the contrary, from the first days of the experiment, and did not revert to the normal value until the 9th day, after which it was somewhat below normal. There was only a slight rise in allantoin content, which in general varied within normal limits.

Fig. 3 illustrates the results found for urinary excretion of uric acid and allantoin at various times after injection of polonium into a group of 4 rats, and for the undernourished control rats. The uric acid content of a 24-hour portion of urine varied normally within the range 0.89-2.67 mg, mean value 1.75 mg; the allantoin content varied within the range 22.6-37.5 mg, mean value 30 mg.

Urinary output of uric acid and of allantoin rose from the 1st to the 3rd day, inclusive, after administration of polonium. During the subsequent 5 days the values fell to normal, or somewhat below. Uric acid excretion fell, and allantoin excretion rose, in the period immediately preceding the death of the animals.

It is of interest that on the 5-6th day after administration of polonium, when uric acid excretion had fallen by 45%, that of the control rats had risen by 50%. This difference is indicative of intensification of the process of oxidation of uric acid at the height of radiation sickness.

In general, the range of uric acid values found in plutonium treated rats was wider than for the control group.

Our results give clear evidence of the effects of radiation, both external and internal, on the contents of the chief end products of purine metabolism in the blood and urine of different species of mammals, and permit the differentiation of these effects from those due to diminished food intake associated with radiation sickness.

SUMMARY

The uric acid and allantoin contents of the blood and urine of dogs and rats receiving lethal doses of γ- and α-radiation have been determined. The uric acid contents of the blood and urine fell by 15-45% during the course of radiation sickness, while the allantoin contents rose by 30-50%. The food rations of the control animals were restricted to those of the irradiated ones, and were quantitatively inadequate; the uric acid content of the blood and urine rose under these conditions by 17-20%, and the allantoin content by 12-15%.

Experiments on rats with a circulatory by-pass of the liver showed that at the height of radiation sickness the liver removed more uric acid from the blood than normally, but put out more allantoin.

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