DISTURBANCES IN THE FUNCTIONAL STATE OF THE LIVER IN DOGS SUBJECTED TO STRONTIUM-90

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Many works have been devoted to studying the functional state of the liver subsequent to the action of ionizing radiation on the organism. A number of authors [4, 7, 8], investigating carbohydrate metabolism in dogs subjected to polonium administration, showed that early disturbances in the carbohydrate metabolism are observed with the acute and subacute course of the disease process, manifested by an elevation of the blood sugar level, and the presence of pathological sugar curves (torpid, double-peaked, irritative, etc.).

The literature devotes much attention to studies of the biological action of Sr^{90} on the organism this being one of the most dangerous fragments of uranium fission, but up until now the investigations have been concerned chiefly with its influence on hemopoiesis [1, 2, 3, 6, 9, 10]. There are little data on changes in the functional state of the liver following exposure of the organism to Sr^{90}.

The purpose of this work was to investigate carbohydrate functioning of the liver dynamically, in dogs subjected to one treatment with Sr^{90}.

EXPERIMENTAL METHOD

The experiments were set up on 10 non-pedigreed male dogs, $1\frac{1}{2}$-2 years of age, weighing 20-25 kg; of these, 7 received Sr^{90} orally, in equilibrium with Y^{90}, using a dose of 1 millicurie per kg, and 3 served as the control.

Sr^{90}, administered in the indicated amount, caused the development of radiation sickness in all the experimental animals. In the first 6-8 days, the clinical symptoms of the disease were manifested weakly. After 20 days, we observed signs of radiation disease: the animals became sluggish, appetite decreased, diarrhea was noted in a number of cases, and we observed a decrease in weight by 10-22% of the original level. After 2-3 weeks the leukocyte count fell by 38%, and the erythrocyte count, by 10%.

On the 29th day following administration of the material, 2 of the experimental dogs died. In the animals that survived the acute period of radiation sickness, there occurred a temporary improvement in general condition.

Beginning with the 40th-50th day of illness, the condition of the animals again worsened markedly. We noted general sluggishness, fur loss, and the appearance of punctate hemorrhages in the mucosa of the mouth and the conjunctiva of the eyes. Over a period of 180 days after the administration of Sr^{90}, the general condition of the experimental animals was moderately severe.

In order to appraise the functional state of the liver, we determined the blood sugar level after loading. Glucose was introduced into the stomach via a sound, using a dosage of 2 grams per kg of the animals' weight, in the form of a 13% solution. Blood was drawn for analysis before the loading, and every 30 min after the loading over a period of $2\frac{1}{2}$-3 hours. The experiments were performed in the morning, on an empty stomach, 18-20 hours after food intake. The concentration of glucose was determined by the anthranone method.

EXPERIMENTAL RESULTS

Before the glucose loading, the blood sugar concentration in the dogs was equal to an average of 74.95 ± 3.01 mg; after the injection of Sr^{90}, it rose every month, and after 90 days, it had increased by 27-44 %.

Blood Sugar Concentration (in mg %) in Dogs Following Sr^{90} Administration

Time of investigation	Before glucose loading	Sugar curve after administration of glucose (in minutes)						Hyperglycemic coefficient (1.3 normally)	Bowden's coefficient (25-30% normally) (in %)
		30	60	90	120	150	180		
Starting data	74,95±3,2	106,8±3,1	101,9±0,9	88,59±3,3	78,83±3,5	68,68±4,1		1,38±0,01	38
Two weeks after Sr^{90} administration	85,2±1,2	121,1±1,3	141,2±1,2	146,1±2,5	144,1±2,01	150,2±1,02		1,98±0,04	98
One month after	86,59±8,1	100,9±19,2	109,31±21,2	104,67±23,6	126,1±3,1	102,32±25,0		1,44±0,09	44
Two months after	86,9±4,7	119,92±17,2	107,71±6,1	102,9±5,1	105,0±2,5	100,33±10,7		1,4±0,03	40
Three months after	95,72±4,9	131,23±6,02	145,72±7,9	121,19±8,8	115,5±8,1	105,65±5,9		1,5±0,012	50
Four months after	92,39±5,1	111,84±4,4	106,01±12,1	90,3±4,6	92,67±5,9	93,35±4,0	89,79±5,0	1,25±0,04	25
Five months after	76,54±1,8	102,19±6,5	113,41±5,5	110,85±1,8	101,12±2,6	95,61±5,0	85,74±6,9	1,5±0,02	50
Six months after	66,39±1,1	88,74±0,8	96,55±1,2	84,9±2,0	83,44±3,3	76,2±0,2	72,73±1,6	1,46±0,08	46
Control	76,1±0,9	101±1,2	98,3±0,9	73,1±0,9	72,1±0,12	65,0±0,1		1,3±0,12	30

In subsequent months, the blood sugar level decreased, and by the 180th day, it was reduced by 8-15% of the original level. Essential disturbances in the carbohydrate metabolism were noted as early as the 14th day after administration of Sr^{90} (see table). At this time, following the introduction of glucose, we recorded a distorted sugar curve, and its character was retained for a rather prolonged period of time (Fig. 1).

The maximum increase in the blood sugar level was shifted from the 30th minute to the 60th, and sometimes to the 90th-150th minute. The amount of sugar in the blood did not return to normal, and even after 3 hours it remained somewhat elevated. In the majority of cases, the hyperglycemic coefficient was greater than normal – 1.45-1.62; in isolated instances (the dog Medyak), it reached 1.82-1.98 in the third month after Sr^{90} administration (see table).

Elevation of the blood sugar level and an increased hyperglycemic coefficient were noted throughout the entire 180 days of observation. Six months after the exposure, although the sugar curve in all the experimental dogs showed a greater slope than in the previous months, the level of sugar in the blood and the hyperglycemic coefficient were still further elevated. The increase in blood sugar concentration apparently indicates an inhibition of the insulin apparatus.

The delayed normalization of the sugar level can be explained not only by pancreatic insufficiency, but also by an increase in sympatho-adrenal tonus, which is indicated by the elevation in the hyperglycemic coefficient.

To appraise the functional state of the liver, we also used the radioisotope method of investigation. For this purpose, we employed a preparation of Bengal red, tagged with J^{131}, with the help of which it is possible to evaluate the functioning of the polygonal liver cells and the condition of the biliary ducts [11, 12, 13]. The preparation of Bengal red was injected into the animals intravenously, using a dose of 0.2 microcuries per kg of body weight, and then, with the aid of the DSU-60 scintillation apparatus, we studied the processes of accumulation and excretion of the radioactive stain by the liver. Examination of the animals was carried out at 4, $4\frac{1}{2}$, and 5 months after administration of the Sr^{90}.

According to our data [5], the radioactivity curve of the liver in dogs has a characteristic form. Within 10-15 sec after administration of Sr^{90}, one notes a rapid rise in radioactivity, due to the entrance of Bengal red into the liver (vascular phase). Then the radioactivity slowly rises, reflecting the absorption of the Bengal red by the polygonal liver cells. The maximum absorption of the stain is noted after 15-20 min.

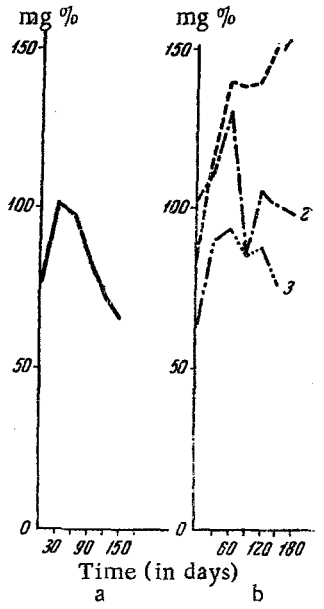

Fig. 1. Glycemic curve before (a) and after (b) the administration of Sr^{90}.
1) After 14 days (K-1, 98/150 min);
2) after 120 days (K-1, 25/60 min);
3) after 180 days (K-1, 46/60 min).

Representing this portion of the curve on a semilogarithmic scale shows that the accumulation of Bengal red by the liver is accomplished as an exponential function.

Following to this graph, it was possible to calculate the constant for the absorption of Bengal red by the liver,

$$\frac{\text{maximum absorption (in impulses)}}{\text{time of maximum absorption (in min.)}}$$

which, under the conditions of our experiment, was equal to 1.5×16 imp per min (Fig. 2,a). Excretion of the radioactive stain into the gall bladder was accomplished rather quickly in the healthy dogs. The time required for half-excretion was equal to an average of 45 min. In the dogs poisoned with Sr^{90}, the accumulation of stain in the liver was reduced, as a result of which the radioactivity curves were considerably lower than in the normal animals. The absorption constant was slightly more than a third of the figure for the healthy dogs. It was difficult to determine the time of maximum absorption of the stain, since the stain that fell into the liver was not excreted into the gall bladder for a long time, and only by the 37th minute did we note a minimal decrease in the activity within the liver (Fig. 2,b).

Thus, the data of the radioisotope method, as well as the results of the biochemical analyses, all indicate that the functional capacity of the liver is markedly disturbed. Especially pronounced changes are observed in the carbohydrate metabolism within the first 14-30 days, i.e., in those stages of development of radiation sickness when there is clear manifesta-

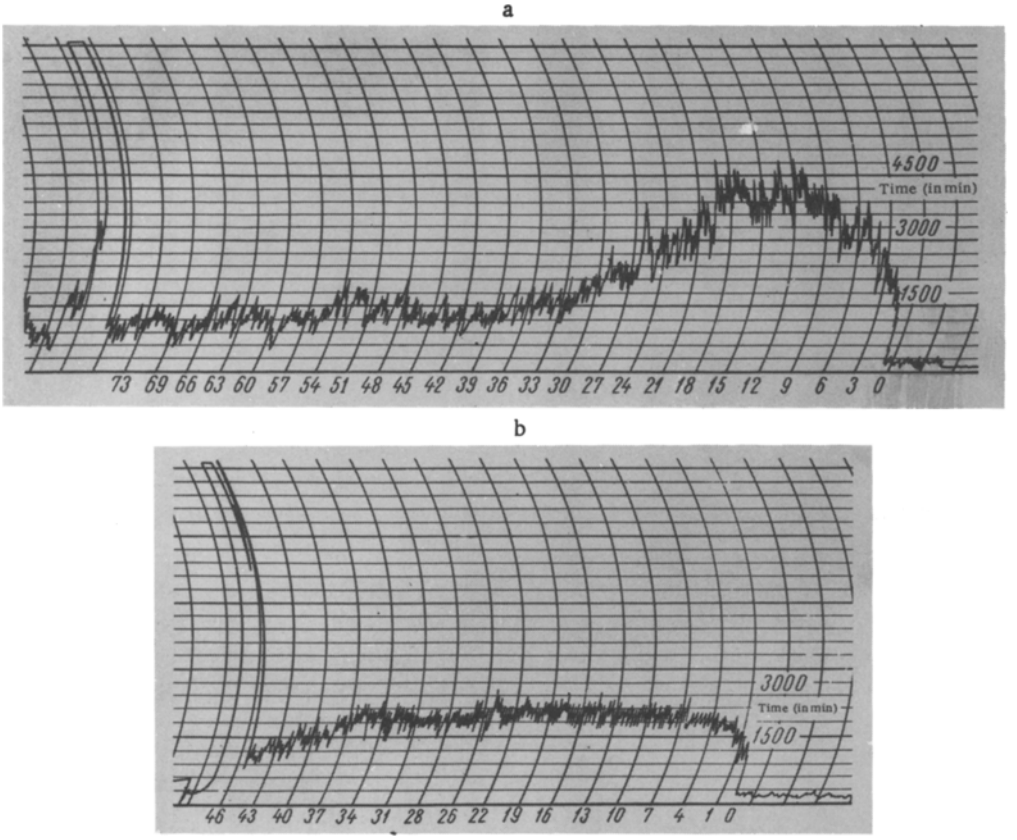

Fig. 2. Radioactivity curves of the liver in a healthy dog (a) and 4 months after the administration of Sr^{90} (b).

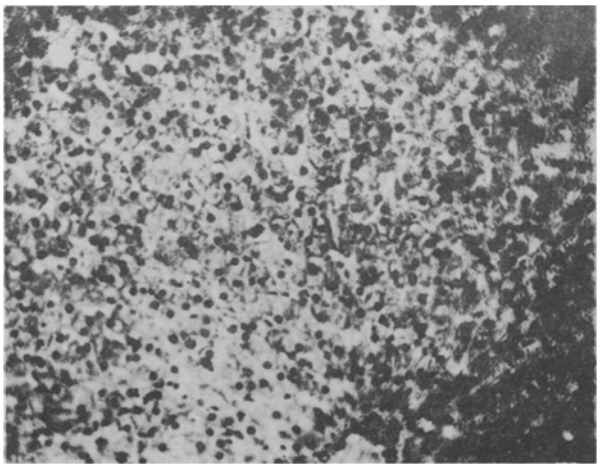

Fig. 3. The liver of a dog, 180 days after the oral administration of Sr^{90}. Stained with hematoxylin-eosin. Magnification 400 ×.

tion of disturbances in the general state of the animals, and when injury of the actual liver tissue also takes place. Morphological investigations of the liver in all the experimental dogs, 180 days after the administration of Sr^{90}, showed that the liver was eroded in certain areas, and we noted dilatation of the vessels, more pronounced in the center of the lobules, and early necrobiosis of individual hepatic cells (Fig. 3).

The liver actively participates in the excretion of Sr^{90} from the organism; according to our data, the activity of the bile on the 90th day after its administration was equal to $23 \pm 0.4 \cdot 10^{-4}$ microcuries/ml.

The total dose of radioactivity created in the liver by the administration of the Sr^{90} was equal to 10-15 rads. It should be noted that with the injection of stain tagged with J^{131}, this dose, one day after the injection, was equal to a total of only 6.3 millirads. Thus, we attribute the observed pathological changes in the liver to the direct action of Sr^{90} on the hepatic tissue.

SUMMARY

Strontium-90, administered orally to dogs in a dose of 1 millicurie/kg, caused disturbances in the carbohydrate metabolism of the liver, changes in the hepatic tissue, and a reduction in bile formation and bile excretion. Pathomorphological investigations demonstrated injury to the liver tissue, dilatation of the vessels (which was more marked in the center of the lobules), and early necrobiosis of individual hepatic cells. The total dose built up by the administration of Strontium-90 (in 180 days) was equal to 10-15 rads.

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