Distribution and Excretion of Electrolytes after Acute Whole-body Irradiation Injury. I. Studies with Radiopotassium.* (19169)

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There has been considerable speculation as to the alterations in body water and electrolytes including potassium that might occur with acute whole-body irradiation injury. There is no conclusive evidence as to the cause of early death in irradiated animals, but there is suggestive evidence that alterations in tissue and blood electrolytes may be important in this regard. Edelmann(1) administered 500, 800 and 1000 roentgens to rats, and noted at all levels an increased urinary excretion of potassium, sodium and chloride on the first and fifth days after irradiation. Failure to find any consistent trends in electrolyte balance, including serum potassium levels following an LD50 exposure in dogs, has recently been reported by Soberman and coworkers(2). However, their report was based on serial analyses of plasma electrolytes without any of the excretory or tissue determinations that should be included in a true "balance" study. Moon has reported a rise in blood potassium levels during radiation sickness(3).

In considering electrolyte alterations in irradiated animals, it is important to realize the differences in sensitivity to irradiation among the various tissues and organs of the human and animal body. Radiosensitivity is probably related directly to the rate at which cells grow and divide. Thus lymphatic tissue, blood, blood-forming organs including the spleen, germinal epithelium and the mucosa of the gastrointestinal tract are considered to be most sensitive to irradiation; liver, kidney, lung and adrenal occupy an intermediate position; smooth and striated muscle, cardiac muscle, brain, nerve and bone are considered to be resistant to irradiation injury(4). Animals dying from irradiation injury may show extensive histopathological changes in sensitive tissues, while other tissues exhibit little, if any, alteration. Our experiments were designated to follow the movement of potassium in irradiated animals.

Methods. Slonaker male rats, weighing approximately 250 g, were fed a synthetic diet which is complete for the rat. Radiopotassium prepared by cyclotron bombardment of argon with alpha particles was kindly supplied by Dr. Joseph Hamilton. Owing to the relatively short half-life of the radioisotopes K^{42} and K^{43}, which are obtained by this procedure, it was necessary to administer tracer doses which alone delivered appreciable irradiation to the control as well as the experimental animals. The animals were injected subcutaneously with the carrier-free radioactive isotopes 24 hours before sacrifice, as it is generally agreed that satisfactory equilibration is obtained in this period. There were 6 groups of 6 rats each—3 control groups and 3 experimental groups. The 3 groups of control animals received a calculated dose of 50, 85 and 175 r.e.p., respectively. The 3 experimental groups of experimental animals were given 830, 819 and 817 roentgens, respectively, by means of the X-ray machine at 215 k.v. and 15 m.a., with 1.2 mm Al and 0.5 mm Cu filters at a rate of 78 r per minute. When the irradiation from X-rays and from K^{42} and K^{43} are added, these groups of animals received a total irradiation dosage of 880 r, 904 r, and 992 r; the LD50 for these animals was approximately 800 r. The irradiation dosage provided by the X-ray machine was verified in each instance with a paraffin phantom and victoreen r meter; control animals were sham irradiated under the

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2. Soberman, R. J., Keating, R. P., and Maxwell, R. D., *Am. J. Physiol.*, 1951, v164, 450.

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TABLE I. Average Values for Radiopotassium Concentration in Tissues and Organs of Rats After Acute Whole Body Irradiation, Expressed as % of Administered Dose per g.

Organ		Days after irradiation or sham irradiation 1	2	3	Significance* Control	Treated	Difference
Blood plasma	C†	.03	.03	.03	No	No	No
	I	.04	.03	.04			
Lymph nodes	C	.74	.68	.60	”	Yes	Yes
	I	.28	.45	.37			
Spleen	C	.74	.69	.71	Yes	”	”
	I	.67	.58	.64			
Stomach	C	.48	.37	.38	”	”	”
	I	.45	.30	.32			
Small intestine	C	.60	.44	.40	”	”	”
	I	.50	.26	.26			
Large intestine	C	.51	.34	.32	”	”	”
	I	.50	.26	.26			
Gonads	C	.56	.54	.62	”	”	No
	I	.57	.50	.57			
Lung	C	.45	.40	.40	”	”	”
	I	.44	.33	.34			
Liver	C	.57	.51	.55	”	”	”
	I	.56	.51	.61			
Kidney	C	.44	.43	.45	”	”	”
	I	.45	.39	.47			
Skin	C	.22	.24	.25	”	”	”
	I	.23	.21	.23			
Brain	C	.43	.42	.47	”	”	”
	I	.45	.40	.41			
Heart	C	.51	.50	.50	”	”	”
	I	.54	.45	.47			
Skeleton	C	.35	.32	.28	”	”	Yes
	I	.33	.21	.22			
Muscle	C	.74	.63	.76	”	”	No
	I	.75	.63	.72			
Red cells	C	.51	.61	.67	No	No	”
	I	.59	.56	.63			
Thymus	C	.79	.89	.47	”	”	Yes
	I	.23	.33	.33			

* Analysis of variance was performed upon data for each organ tabulated to determine whether the day to day changes in control or treated groups were significant. In addition the significance of the difference between the control and irradiated groups was checked. The results are given in the appropriate columns. A "yes" in the "control" or "treated" column, for example, indicates a significant change ($P = .05$) in concentration of K during experiment. A "yes" in the column headed "difference" indicates a similarly significant change in concentration of K in irradiated animals as compared to controls.

† C = control; I = irradiated.

X-ray machine for a time period similar to that for the exposed animals and in the same containers. The experimental and control animals were sacrificed at 24, 48 and 72 hours after irradiation and sham irradiation.

The rats were housed in standard metabolic cages. Urine and feces were separated and their volumes measured. At the time of sacrifice, the animals were anesthetized with ether, and heart blood was withdrawn into a heparinized syringe. The animals were then sacrificed by means of additional ether and the various tissues cleanly removed. The contents of the gastrointestinal tract were removed and the tissues were rinsed carefully in Tyrode's solution after which they were blotted dry on filter paper. All samples were weighed wet, assayed for radioactivity with a crystal counter and calculated as per cent of the administered dose per 24-hour specimen of urine or feces, or per gram of tissue.

Results. Radiopotassium concentrations per

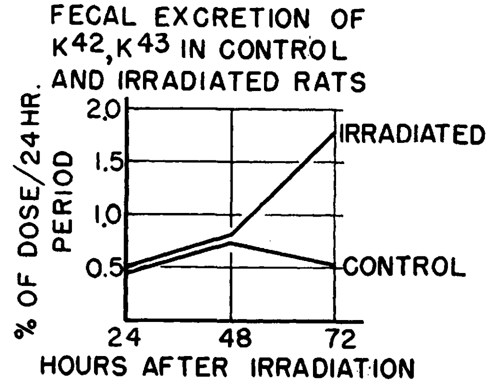

FIG. 1.

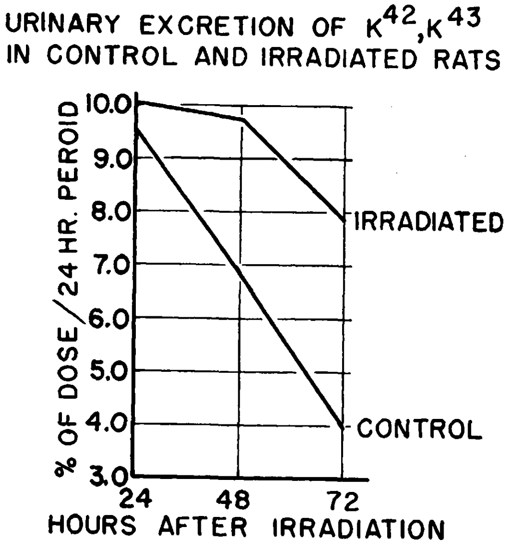

FIG. 2.

gram of tissue for a number of organs and tissues and the results of an analysis for variance are listed in Table I. The lymph nodes, thymus, spleen, stomach, small intestine, large intestine and bone exhibited a significant difference between control and heavily irradiated groups, as manifested by a reduction in the concentration of radiopotassium in the heavily irradiated group. The gonads were the only "sensitive" organ which did not follow this pattern, perhaps due to the comparatively small amount of "sensitive" germinal epithelium present. Fecal excretion of radiopotassium rose sharply with the onset of diarrhea at 72 hours post-irradiation (Fig. 1); urinary potassium levels were increased in the irradiated animals throughout the experiment (Fig. 2).

Discussion. Interpretation of our findings cannot include partition of potassium between extracellular and intracellular compartments since the data are calculated on a wet weight basis. Further studies have been initiated which it is hoped will furnish information necessary for more precise considerations of electrolyte partition.

In the subsequent paper in this series we report our results in generally similar experiments with radiosodium, and since these are closely related, some of the discussion is deferred to that paper. Several of our findings, however, deserve mention here.

On the basis of histopathological evidence, bone is reported to be a radiation-resistant tissue. Accordingly, we were impressed by the loss of potassium from bone in the irradiated animals. To determine whether this potassium was lost from bone, bone marrow or both, Dr. Virginia Davenport kindly carried out potassium determinations (flame photometer) on whole femur and on tibia with the marrow removed. The results (Table II) indicate that while there was a substantial loss from bone marrow—a sensitive tissue—there was the same degree of loss from bone with marrow removed. We assume that this may indicate a movement of potassium out of the bone lattice or a loss of potassium from osteoblasts, which are considered to be the most sensitive of the bone cells. If the latter explanation is correct, our data would suggest that osteoblasts are as sensitive to irradiation injury as are the cells of the hematopoietic system.

Dehydration, diarrhea, total anorexia and shock accompany whole-body irradiation injury in humans, and each of these manifestations has been reported to be associated with a depletion of intracellular potassium, particularly in muscle(5,6). In view of the severity of these manifestations in irradiation injury, we were impressed by our inability to detect more significant changes in potassium concentration in muscle during the 72 hours of the experiment.

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TABLE II. Total Potassium Content of Whole Bone and of Bone With Marrow Removed in Control and Irradiated Rats.*

Bone	Dry bone, m.Eq/kg		Fresh bone, m.Eq/kg	
	Control	Irradiated	Control	Irradiated
Whole femur	57.9	37.5	34.2	22.5
Tibia (marrow removed)	20.2	13	11.8	7.8

* As determined by flame photometry.

Urinary determinations, when compared with the control data, suggest that the potassium moving out of a number of tissues appeared rather promptly in the urine, and that the kidney does not conserve potassium in situations of developing intracellular deficit. Thus, total anorexia, depletion of potassium in a number of tissues and increased loss in stools and in the urine, all contribute to the fact that these animals were in absolute potassium deficiency.

Summary. Rats show a substantial loss of potassium from a majority of radiosensitive tissues beginning within 24 to 48 hours after irradiation. There is a comparable loss of radiopotassium from bone. Radiopotassium excretion is increased in the urine of irradiated rats, and there is a rise in fecal levels with the onset of diarrhea. It is evident that rats that have been irradiated at over an LD50 level develop an absolute potassium deficiency.

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Distribution and Excretion of Electrolytes after Acute Whole-Body Irradiation Injury. II. Studies with Radiosodium.* (19170)

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Several investigators have reported alterations in the sodium metabolism after acute whole-body irradiation injury. In rats, Painter(1) found an expansion of sodium space in the total animal and in the gastrointestinal tract five days after an LD50 exposure. Bennett *et al.*(2) noted a retention of radiosodium in rats with as much as 2% of the total dose accumulating in the gastrointestinal tract and smaller amounts in the kidney and spleen after an LD50 exposure. In the experiments of Bennett *et al.*, serum sodium levels rose by 5-8 mEq., and Kohn(3) has reported a plasma sodium rise of 3 mEq. on the 4th day after exposure just below an LD50. Soberman *et al.*(4) were unable to detect any significant alterations in plasma sodium in the dog after an LD50 exposure. Other investigators have reported a rise(5) or a fall(6) in blood sodium levels after irradiation injury.

This report concerns the pattern of urinary and fecal excretion of sodium in rats after acute whole body irradiation with X-rays and the accompanying alterations in sodium concentration in a number of tissues and organs.

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