TABLE 1

THE SOLUBILITY OF THE FIBRIN CLOTS PRODUCED BY THROMBIN OR BY *Bothrops atrox* VENOM

Components of the experiments	1*		2*		3*		4*		5*	
Fibrinogen	×	×	×	×	×	×	×	×	×	×
Serum	×	×								
Oxalated serum					×	×				
Inactivated serum									×	×
Ca ions	×	×					×	×		
Thrombin	×		×		×		×		×	
Venom		×		×		×		×		×
Result	−	++	+	+++	+	+++	+	+++	+	+++

* Symbols have the following meanings:
× marks in each column the components used in any one experiment; − insoluble; + soluble; ++ very soluble; +++ spontaneous solution.

the coagulating action of snake venom are influenced in their solubility by the two factors mentioned by Laki and Lóránd. The technique of the tests was similar to that of Lóránd, though smaller quantities were used than those mentioned by him (*4*). *Bothrops atrox* venom solution was used in such concentration as to give similar clotting times to those obtained by thrombin. The concentration of the urea solution was 60% and was added in volume equal to that of the reaction mixture; this mixture consisted of fibrinogen, the clotting agent, and one or two additional components, these being, in turn, serum, oxalated serum, serum inactivated by heat and $CaCl_2$ solution. When one of the additional components was excluded from the mixture saline was added to keep the volume of the mixture constant; a veronal buffer was used to maintain the pH of the mixture at 7.2. It was found that all the fibrin clots formed by the coagulating activity of the *Bothrops atrox* venom were soluble even though Ca ions and the serum factor were present. At the same time Lóránd's results were confirmed, since the clots formed by thrombin in the presence of the two factors were insoluble. The fibrin obtained by snake venom dissolved readily in all cases, and spontaneously when one of the two factors was absent. This cannot be stated of the clots formed by thrombin (Table 1).

Although, when observed with the naked eye, there seems to be no difference between the fibrin clots produced by either of the two agents, there probably is a difference in the degree of their polymerization, i.e., in their molecular structure. This might also explain the difference in their solubility.

The difference in the solubility of fibrin clots produced by thrombin and by venom offers further evidence in support of the opinion presented elsewhere (*1, 2*) that the clotting agent in the snake venoms of the *Bothrops* species is different from thrombin.

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Effect of Evisceration on Renal Glycogen

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The kidneys of eviscerated, hepatectomized rabbits, rats, and dogs were shown to contribute glucose to blood (*1, 2, 4–6*). Although it has been assumed that renal gluconeogenesis is the process responsible for this source of blood sugar, renal glycogen as a precursor has not been excluded. By determining serial kidney glycogen values in eviscerated, hepatectomized dogs, one of these possibilities could be excluded. If original renal glycogen values were great enough and sufficient renal glycogen disappeared, this storage form of carbohydrate could be assumed to play some role in maintaining blood sugar.

Accordingly, kidney glycogen values were determined immediately, and 1½–2½ hr after evisceration and hepatectomy in normal and diabetic dogs. After evisceration, the blood sugar was allowed to fall spontaneously, since it has been under these conditions that the kidney has been shown to contribute glucose to blood. The techniques for pancreatectomy, evisceration, and hepatectomy, and for the chemical analysis of the specimens were described previously (*2, 3*).

TABLE 1

KIDNEY GLYCOGEN AND BLOOD GLUCOSE VALUES IN NORMAL AND DIABETIC EVISCERATED, HEPATECTOMIZED DOGS IMMEDIATELY AND AT VARIOUS TIME INTERVALS AFTER EVISCERATION

Normal dogs	Time after evisceration (min)	Kidney glycogen (g %)	Blood sugar (mg %)
No. 1	0	0.026	64
	70	0.030	16
No. 2	0	0.025	82
	120	0.028	23
No. 3	0	0.031	80
	105	0.043	20
Diabetic dogs			
No. 1	0	0.099	270
	120	0.109	144
No. 2	0	0.079	257
	150	0.108	135
No. 3	0	0.097	336
	125	0.103	170

As can be seen from Table 1, it is impossible to account for the glucose released by the kidney on the basis of the glycogen originally present in these organs. Thus the immediate postevisceration biopsies of kidneys reveal only about 0.05 g of glycogen/100 g of kidney tissue in normal dogs and about 0.1 g of glycogen/100 g of kidney tissue in diabetic dogs. If this glycogen were to serve as a source of blood sugar, the total amount present

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(approximately 50 mg) could in no way account for the amount of glucose contributed by renal tissue. As can be seen from the data, renal glycogen did not disappear but increased slightly in amount during the period glucose was being released into the blood stream. It is obvious, therefore, that the glucose contributed to blood by the kidney arises from noncarbohydrate precursors. The renal output of glucose is larger than can be attributed to temporary storage of glucose as glycogen with subsequent glycogenolysis and release of glucose to the blood stream.

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The Effect of Exercise upon the Lethality of Roentgen Rays for Rats

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The extent of biological damage resulting from exposure to roentgen rays can be altered by physical and chemical measures that alter the metabolic level of the test organism. The mortality rate of irradiated homeothermic animals can be increased by exposure to the physical stress of a hypothermic environment following irradiation (*6*, *10*). Irradiated poikilothermic organisms, such as fertilized *Ascaris* eggs (*3*), frogs (*9*), chick embryos (*11*), and newborn rats (*4–6*), show evidence of greater resistance or repair when kept at low temperature. In several of these studies (*3–5*, *11*), the lowered metabolic activity of the organism is indicated as the explanation for increased resistance to radiation. It is of interest to note that anoxic conditions favor survival of organisms and enhance tissue resistance to radiation (*1*, *5*, *8*).

Treatment of mice with thyroxine greatly increases the lethality of a given dose of ionizing radiation—an increased oxygen consumption was also demonstrated (*2*). Kirschner *et al.* (*7*) demonstrated that rats that died following potentially lethal doses of x-rays had higher postirradiation metabolic rates than those that survived, although both groups showed rises above normal.

Such studies suggest that conditions tending to increase the metabolic rate would also increase the lethal effects of roentgen rays. In order to investigate further the role of metabolic level in determining radiosensitivity, vigorous exercise was selected to provide a physiological means of increasing the metabolic rate as an alternative to stimulation by drugs or changes in the physical environment of the organism.

TABLE 1

TOTAL MORTALITY TO RATS* FOR EACH DOSE LEVEL OF X-RAYS DELIVERED TO THE WHOLE BODY

	Not irradiated, exercised	Irradiated, not exercised	Irradiated, exercised
600 r			
Initial No.	18	30	26
No. died	0	0	13
% Died	0	0	50
700 r			
Initial No.	26	38	26
No. died	0	13	24
% died	0	44	92
860 r			
Initial No.	21	30	33
No. died	0	25	33
% died	0	83	100

* Animals were observed for 90 days.

Male rats of Sprague-Dawley strain bred in this laboratory were used throughout this study. For each dose level studied, all animals were from litters whelped at approximately the same time and were of similar weight (± 8%). The exercised animals performed a standardized exhaustive exercise test for rats, which was developed in this laboratory (*12*). In this test, they were allowed to swim individually in tanks of water until they were exhausted. The animals were exercised for ten trials prior to irradiation in order to adapt them to the conditions of testing. After irradiation they were exercised daily, five times per week throughout the study. At each radiation-dose level employed, nonirradiated animals were exercised concurrently with the irradiated animals, but no deleterious effects of the performance test per se were observed. The duration of exercise was found to be 15–30 min per trial with a weight load of 10 g attached to each animal.

Because the number of animals that could be exercised per day was limited, irradiation at each dose level was performed on different days and with slightly different radiation factors, as follows: Radiation factors for 600 r were: 250 kv x-rays, 15 ma; 1.3-mm copper filter; target distance, 27 in.; 25 r/min air dose. For 700 r and 860 r the factors were: 240 kv x-rays, 8 ma; 0.6-mm copper filter; target distance, 39 in.; 8.5 r/min air dose.

After irradiation with 600 r, 50% of the exercised rats died, and all nonexercised irradiated rats survived (Table 1 and Fig. 1). Exhaustive exercise of less than 30-min duration per day was sufficient to induce a 50% mortality at this dose of x-rays. At a dose (700 r) that was somewhat lethal (44%) to nonexercised animals, there was a doubling in the incidence of mortality (92%) among exercised animals. At a highly lethal dose (860 r), animals that were exercised showed symptoms of roughened coat, diarrhea, and crusted nares much sooner after irradiation than did their nonexercised controls. With

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