

# THE INFLUENCE OF DRUGS ON TOXICITY ACQUIRED BY SERUM THROUGH EXPOSURE TO IONIZING RADIATION

V. V. Alpatov and A. V. Shubina

From the Radiological Department (Head—Professor A. V. Kozlova) State Scientific  
Research X-ray Institute (Director—Professor I. G. Lagunova)

Presented by Active Member AMN SSSR V. V. Parin

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In animals, acute radiation sickness is associated with an increased toxicity of the blood serum, which is measured by the survival of paramecia placed in an aqueous solution of the serum [1, 2].

The object of the present investigation has been to study the action of a number of drugs on the toxicity of serum from an irradiated animal.

This line of research has been dealt with only to a very small extent in published reports. We may note the works of Macht [4] and Macht and Gardner [3] on this subject.

## METHOD

A study of the toxicity of the blood and serum was made at various times on 17 dogs, 12 of which received a dose of 600 r, 2 one of 700 r, while 3 were not irradiated; 11 rabbits were also used, of which 4 received 800 r and 7 were not irradiated; of 50 rats, 20 received 800 r, and 30 were not irradiated. Blood was taken from the animals, which had been used by E. A. Abaturova, A. B. Shubina and G. N. Elpat'evskaya in a study of the action of a number of drugs on the course of radiation sickness. We measured the toxicity of serum of animals which had received a single total irradiation dose from an RUM-3 apparatus under the following conditions: voltage 180 kv, current 15 ma, filters 0.5 mm Cu and 1 mm Al; for dogs, the distance from the skin to the focus was 100 cm, for rabbits 70 cm, and for rats 40 cm. After irradiation, the animals were given 'leukogen', 'caferid', batyl alcohol and selachyl alcohol, to test the therapeutic action of these substances.

Toxicity of the serum and of the blood was measured by their action on the slipper animalcule (Paramecium caudatum). The paramecia were placed on object glasses in three drops, each of which contained five paramecia, and five drops of the blood or serum solution were added. Altogether 30 paramecia were used for each experiment (two object glasses). The slides were placed in a moist chamber, consisting of a Petri dish; the Petri dishes were placed in a crystallizing basin, covered with a second similar basin, and then placed in a thermostat at 25°. After 24 hours, a count was made of the paramecia, and their number was expressed as a percentage of the original count. The toxicity was expressed as the percentage of the animals which died, or as the percentage increase. In each experiment, as a control, paramecia were placed in the medium in which they were grown in the laboratory; it consisted of boiled water to which brewers' yeast had been added. In all the experiments, a total of more than 11,000 paramecia were used, and the extent of the increase or the number of animals which died were counted. We measured the toxicity of blood at different times after irradiation. Blood or serum from rats was used in a dilution of 1 : 200 (i.e. a 0.5% solution), while for the remaining animals the dilution was 1 : 20 (i.e. a 5% solution). Blood and serum were diluted with boiling water.

We carried out toxicity tests for blood and serum taken from the same animal. It was then found that the blood was not toxic, i.e. as a rule the paramecia did not die in the blood solutions. Therefore, the later experiments were carried out only with blood serum. We measured the toxicity of the serum in both irradiated and non-irradiated animals.

## RESULTS

From the experiments as a whole it was found that the blood serum of the different animals had different degrees of toxicity, as shown by tests on paramecia: the serum, and even the blood, of rats caused death of all the

paramecia, even in a dilution of 1 : 100. It was only in the 0.5% solution of the serum that some increase in the number of paramecia was observed, when their number increased by 40 - 50%. However, for the dog and rabbit the "threshold of toxicity" was considerably higher: the paramecia multiplied well in 5% and even in 10% serum solutions. Experiments were carried out with the blood serum of three dogs, seven rabbits, and 30 rats. The animals received the preparation 'caferid,' 'leukogen,' and selachyl and batyl alcohol, as well as the following combinations: batyl alcohol + 'caferid,' batyl alcohol + 'leukogen.' It was found that when the rats were treated with batyl alcohol combined with either 'caferid' or 'leukogen,' the increase in paramecia was 40-80% greater than for the control group. Batyl alcohol increased the multiplication in rabbit blood serum throughout the whole period that the drug was given (30 days). For example, in the serum of rabbit No. 10, before batyl alcohol had been given, the increase in the paramecia had been 15%, but afterwards, for a whole month, it increased to 96% (Table 1).

TABLE 1. Influence of Blood Serum of Rabbit No. 10 (which received batyl alcohol) and of Rabbit No. 2 (which received selachic alcohol) on the Multiplication of Paramecia (in percentage).

Number of rabbit	Before the preparation was given	After the preparation was given				
		1st day	3rd day	7th day	15th day	30th day
10	+ 15	+ 23	+ 36	+ 71	+ 80	+ 96
2	+ 26	+ 10	0	+ 40	+ 52	+ 128

Immediately after the rabbits and dogs had been treated with selachyl alcohol, the multiplication of the paramecia was depressed for the first three days, but later recovered sharply (see Table 1).

For the experiments on the toxicity of the serum of irradiated animals, we used the blood serum of 14 dogs, 4 rabbits, and 20 rats, all of which had been irradiated. Of these animals, 6 dogs, 1 rabbit, and 5 rats were the irradiated controls, while after irradiation the remainder were treated with the preparations described above. After irradiation, in all the animals of the irradiated control group there was a considerable increase in the toxicity of the blood serum, so that most of the paramecia died. As can be seen from Table 2, three days after irradiation, in

some of the dogs up to 98% of the paramecia died. After a short period when toxicity was reduced, by the 6th-7th day it once more rose, and later returned with some fluctuation to the original level, or else was maintained somewhat below this value for 30-36 days after irradiation.

When the drugs were given, the toxicity of the serum was not so marked in the first few days after irradiation as it was in the irradiated control group: there was a negligible death of the paramecia - not more than 30 - 40%, or else their multiplication was inhibited (Table 2).

TABLE 2. Toxicity of Dog Serum, in Percentage (irradiation dose 600 r)

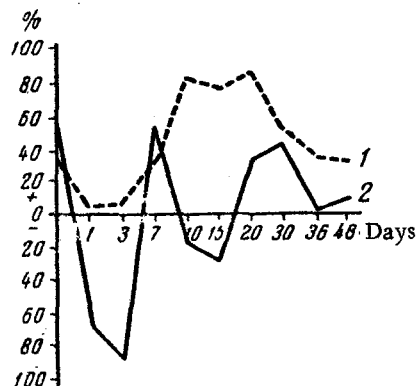
Time in days	Irradiation control		'Leukogen' + 'caferid'		Selachyl alcohol + 'caferid'	
	No. 1	No. 2	No. 7	No. 8	No. 10	No. 11
Before irradiation	+ 35	+ 42	+ 27	+ 38	+ 40	+ 26
After irradiation						
1st	- 56	- 82	0	- 42	+ 32	+ 18
3rd	- 78	- 98	+ 3	- 30	+ 51	+ 15
7th	+ 32	+ 75	+ 15	+ 120	+ 3	- 1
10th	- 40	+ 12	+ 70	+ 156	+ 81	+ 30
15th	- 10	- 38	+ 108	+ 95	+ 65	+ 57
20th	+ 36	+ 35	+ 86	+ 120	+ 43	+ 99
30th	+ 20	+ 68	+ 60	+ 63	+ 31	+ 76
36th	+ 46	+ 20	+ 10	+ 51	+ 43	+ 52
48th	-	+ 38	+ 23	-	+ 29	+ 50

Thus, in the serum of dog No. 7, which received 'leukogen' with 'caferid,' none of the paramecia died after irradiation, and the only change was that for the first three days their multiplication was arrested. In the serum of dog No. 8, during the first 24 hours after irradiation, only 42% of the paramecia died. At later dates, in the serum

of the treated dogs there was an increased multiplication of paramecia, which reached its maximum after 10 - 15 days, after which the reaction of the paramecia gradually returned to normal (see figure, mean values).

We were not able to observe differences between the reactions of paramecia treated with sera of animals receiving different preparations.

A study of the toxicity of the serum, as determined on paramecia, may serve as a prognostic indication. However, this reaction is not specific for radiation damage. Thus, in the serum of the dogs which eventually died, 100% of the paramecia died quite early after irradiation. However, a high mortality of up to 100% in the paramecia was found to occur under the influence of blood serum in nonirradiated dogs which were seriously ill (general condition poor, high temperature, blood-stained vomit).



Influence on the multiplication of Paramecium caudatum of the blood serum of (1) treated and (2) untreated dogs, which had received 600 r of radiation.

#### SUMMARY

It had been observed previously by Genes that the serum of animals treated with ionizing radiation acquires a toxicity which may be detected by the use of Paramecium caudatum as a test organism. The present investigation was carried out on dogs, rabbits, and albino rats, and four drugs (leukogen, caferid, and batyl and selachyl alcohols). These drugs rendered the serum of nonirradiated animals more favorable to the survival and reproduction of paramecia. The increase of the serum toxicity in the nonirradiated animals was less pronounced when the drug had been given.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.