EFFECT OF ENTERAL VACCINATION ON RADIORESISTANCE OF MICE

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Enteral vaccination of mice with a heat-killed culture of Salmonella breslau, carried out according to a particular scheme, increases the resistance of animals to subsequent irradiation. The survival rate of the animals is increased by 10-80% compared with the control. Variants of vaccination performed 4 and 7 days before irradiation were most effective.

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Preliminary vaccination has a favorable effect on the course and outcome of radiation sickness [4]. Not only the intact bodies of microorganisms, but individual components of complete antigens, such as specific polysaccharides and lipopolysaccharides [1], have a radioprotective action [1]. Most investigations on the effect of vaccines on radioresistance have involved parenteral administration of the antigen. However, the enteral method of administration of vaccines is the most areactive and has several advantages over the parenteral method: protection of the portals of entry, rapidity of the creation of immunity, breadth of cover of the population.

Few investigations of the effect of oral vaccination on the radioresistance of animals have been described in the literature. Preliminary enteral administration of an Escherichia coli vaccine was shown to lower the survival rate among irradiated mice [3]. Other workers [12] observed an increase in the mean life span to 16.8 days (8.3 days in the control) of mice fed before and after irradiation (γ-rays, 1000 R) with a living culture of E. coli resistant to irradiation and to the action of hydrogen peroxide. Since it has recently been shown [5-9] that enteral vaccination causes considerable immunologic changes throughout the body, without complications attendant upon administration of the antigen, it was to be expected that oral vaccination would have a favorable effect on the outcome of radiation sickness in animals.

The object of the present investigation was to study the effect of enteral vaccination on the radioresistance of animals.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred albino mice, both males and females (1943 mice). The enterovaccine used was a heat-killed agar culture of Salmonella breslau No. 3397. To promote absorption of the vaccine, bile (5-10%) and ethyl alcohol (5-10%) were added to the bacterial suspension after heating. In addition, the cell suspension was made up in bactericidal fluid [10]. The vaccine was injected by means of a curved needle with a solid metallic thickening at its end. A dose of vaccine of 10 billion bacterial cells (0.2 ml) was found to be well tolerated and effective. Doses of 25 and 50 billion bacterial cells caused considerable slowing of the gain in weight by the animals when given repeatedly (over a period of 5-7 days), and for this reason in most experiments a dose of 10 billion bacterial cells per mouse was used. The vaccine was usually given in the morning before feeding, although the animals were not fasted strictly, the reason being that certain food components promote absorption of antigen [2, 11].

The animals were irradiated with x rays from a type RUM-3 apparatus in a dose of 550 R under standard conditions (180 kV, 15 mA, dose rate 20.8 R/min, filter 0.5 mm Al, focal length 50 cm), and with γ rays from a type ÉGO-2 apparatus (dose rate 194-170 R/min) in a dose of 725 R. Altogether 55 experiments were performed, 22 using the RUM-3 apparatus and 33 using the ÉGO-2 apparatus as radiation source. The survival rate of the animals was determined in percent 30 days after irradiation. Unvaccinated irradiated mice served as controls.

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TABLE 1. Effect of Preliminary Enteral Immunization on Survival Rate of Mice after Irradiation

Time interval from end of immunization until irradiation	No. of vaccinations	No. of experiments	No. of mice			χ^2	P^1
			Total	Surviving	Percent of survivors		
1–2 h	1	4	96	31	32	3,8	>0,05
1 day	1	4	96	28	29	1,7	>0,05
	1	6	150	63	42	23	<0,001
4 days	Two cycles, each of three days	2	56	4	7	—	—
	Daily for 4, 7, 14 days	3	89	37	41,5	12	<0,001
	1	7	221	86	38,9	22,1	<0,001
7 days	Two cycles, each of three days	6	320	127	39	13,4	<0,001
	Daily for 6–7 days	4	78	38	48,7	7,1	<0,01
	1	4	157	38	24	—	—
14 days	Two cycles, each of three days	5	245	92	37,5	5,4	<0,02
20 days		3	79	15	19	—	—
Control			775	179	23	—	—

[1]Statistical significance calculated relative to combined data for control group of mice.

Since we know from published work on the study of the effect of vaccination on radioresistance that the course and outcome of radiation sickness in vaccinated animals depends on the dose of vaccine given, the order of combination of vaccination and irradiation, and the length of the interval between them, different variants of combinations of vaccination and irradiation were tested.

EXPERIMENTAL RESULTS

As Table 1 shows, enteral immunization affected the survival rate of the irradiated animals. In many experiments, a statistically significant increase in the percentage of animals surviving after irradiation was obtained only through the action of enterovaccine, although no other protective agents were used. Clearly the outcome of the experiment depended on the length of the time interval between the end of vaccination and irradiation. The best results were obtained when this interval was 4 and 7 days, in the case of single and repeated daily immunization, and 7 and 14 days if the vaccine was given as two preliminary cycles, each lasting 3 days.

Vaccination which ended 1-2 h or 1 day before irradiation, or at longer time intervals (14 and 20 days) before irradiation in most experiments did not produce a significant increase in the survival rate of the irradiated animals. Oral immunization given after irradiation likewise had only a slight effect on the survival rate of the irradiated animals. Hence, in the majority of experiments variants of vaccination carried out 4 and 7 days before irradiation proved effective. The fact was noted that in some experiments, in which mortality among the control animals was 100%, up to 20% of vaccinated animals survived. In some experiments a single dose of enterovaccine before irradiation was more effective than repeated doses: the survival rate among the experimental animals was 15 times greater than in the controls. After repeated administration of antigen, results such as these could not be obtained.

According to information in the literature [3], in the case of parenteral administration of antigen also, single doses are more effective than repeated, and an increase in the dose of vaccine does not increase its effectiveness. Our results showed that an increase in dose of enterovaccine to 25-50 billion bacterial cells, for a single dose, and increasing the total dose to 140-350 billion bacterial cells in the case of repeated vaccination, caused no significant increase in the survival rate. The initial body weight of the mice (19-26 g) had no effect on the experimental results.

Hence, the resistance of animals to irradiation can be increased by preliminary enteral administration of vaccine. This is shown by an increase in the number of mice surviving until 30 days after irradiation, and

it depends on the manner in which vaccination and irradiation are related in time, on the length of the time interval between the end of immunization and irradiation, and also on the number of vaccinations.

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