CHAPTER 23

SENSITIVITY OF IRRADIATED ANIMALS TO INFECTION

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Abstract: The study was carried out to investigate the combined action of γ-radiation and infection on mice. Death rate of animals was estimated in dependence of radiation and vaccination doses.

Keywords: γ-radiation; *Francisella tularensis*; mice

Introduction

One of the main causes of death due to radiation-induced damage is development of endogenous infection at the early period of clinical manifestation of acute radiation disease. On the other hand, the decrease of immunological reactivity of the body following the action of ionizing radiation may aggravate deleterious effects of such kind of weapon of mass destruction as biological weapon (World, 2004; Casadeval and Pirofski, 2004). Easiness of production and spreading, delayed beginning of the disease, diagnostic difficulties make rather real to consider microorganisms as a powerful biological weapon. The use of live vaccine after radiation impact may lead to dissemination of infection in the vaccinated organism.

Exposure to relatively low radiation doses (<1 Gy to a human) causes suppression of immunoreactivity and antibacterial resistance. Risk of infectious disease caused by extremely dangerous pathogens is known to be higher in those exposed to radiation compared to unexposed subjects (Brook et al., 2004, 2005; Elliot et al., 2002).

The most dangerous pathogens are *Variola major, Bacillus anthracis, Yersinia pestis, Clostridium botulinum, Francisella tularensis*. A vast amount of information about extremely dangerous infections, improvement of countermeasures and medical preparedness for and response to pathogenic

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infections has been published for the recent years. However, whether the low resistance to vaccine cultures associates with specific immunoreactivity and what effect will be produced by vaccine culture on a exposed human should be the subjects of further studies.

Experimental results which allow quantification of relationship between dose and sensitivity of irradiated animals to extremely dangerous pathogens may be of significant importance for medical proposes and preparedness.

This study was aimed at investigation of the influence of total γ-irradiation in non-lethal doses on the course of vaccination process in mice.

Material and Methods

White non-linear mice served as biological objects. Certificated strain No 15 *F. tularensis* (Research Institute of Experimental Genetics, Moscow) with high level of "residual virulence" for these animals was used in the experiments. 30 mice were exposed to 1 Gy, 30 mice to 4 Gy, and 30 mice served as a control group (non-irradiated animals). Following 5 days after irradiation the mice were vaccinated subcutaneously with immunization doses 3.2×10^1, 3.2×10^2, and 3.2×10^3 of tularemia cells (per 10 animals for each dose in all three groups). Animals were exposed to γ-radiation at a dose rate 10 cGy/min. In other experiments animals were vaccinated with immunization dose 1.5×10^4 in 26 days after irradiation with dose 4 Gy (%).

Results

Surveillance over the animals during 20 days after vaccination demonstrated an aggravation of vaccination process in the exposed animals by criteria of mortality and life-shortening. The highest mortality in control groups (vaccinated with 3.2×10^3 *F. tularensis*. cells, non-irradiated) and in the group of irradiated (1 Gy) and vaccinated mice was observed on the 8th day following vaccination. The highest mortality in the group of mice irradiated with dose of 4 Gy was observed on the 7th day after vaccination (Fig. 1). Increase in dose of vaccine caused death of irradiated mice on the 6th day and the highest mortality in the control group was observed on the 8th day after vaccination (Fig. 2). Dose of 3.2×10^3 *F. tularensis*. cells caused the highest death of mice in control and irradiated groups on the 6th day following vaccination, i.e. the interval between exposure to agents (radiation and vaccine) and death of mice reduced (Fig. 3).

The results point that the toxicity effect of vaccination took place in the first week after irradiation (Table 1).

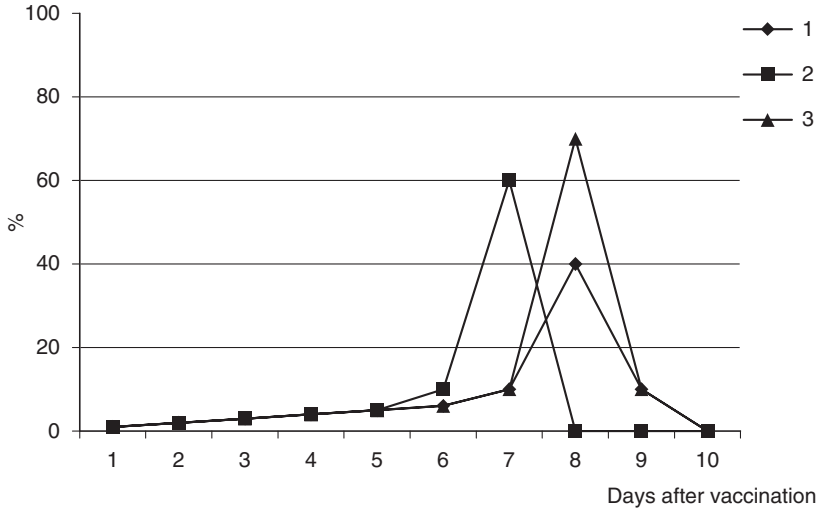

Fig. 1. Mortality in mice (control group and irradiated with different doses) following inoculation of 3.2×10 *F. tularensis* cells (%). 1−3.2×10; 2−4 Gy + 3.2×10; 3−1 Gy + 3.2×10

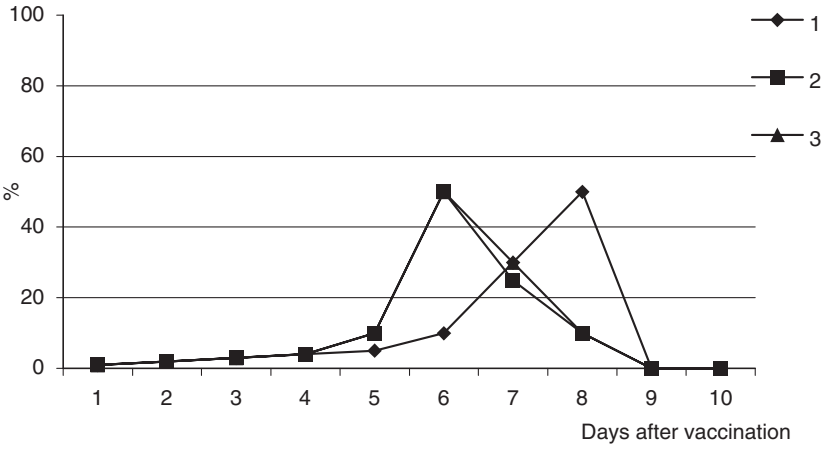

Fig. 2. Mortality in mice (control group and irradiated with different doses) following inoculation of 3.2×10^2 *F. tularensis* cells (%). 1−3.2×10^2; 2−4 Gy + 3.2×10^2; 3−1 Gy + 3.2×10^2

In the next row of experiments the influence of vaccination (its virulence) at the survival of mice injected with tularemia cells after 26 days following whole-body exposure to 4Gy was studied in period reconvalescens (Table 2). Experiments were repeated three times. Vaccinated in the same doses non-irradiated mice served as a control (Figs. 4–6).

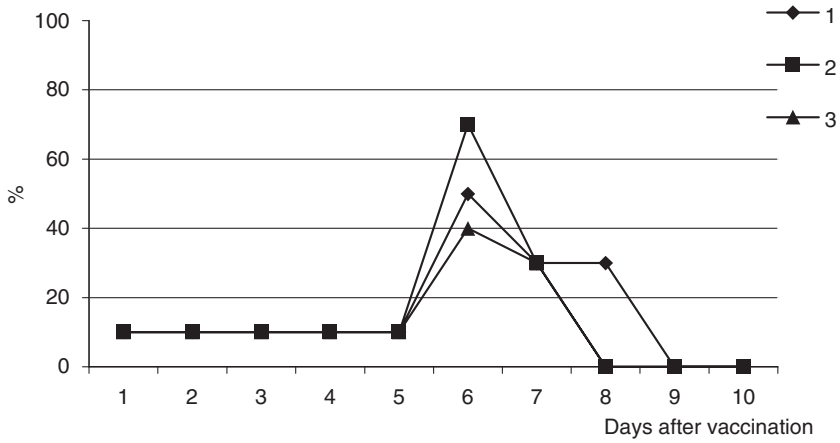

Fig. 3. Mortality in mice (control group and irradiated with different doses) following inoculation of 3.2×10^3 *F. tularensis* cells (%). 1−3.2×10^3; 2−4 Gy + 3.2×10^3; 3−1 Gy + 3.2×10^3

TABLE 1. Lifespan of mice in control and irradiated groups following vaccination with *F. tularensis* cells in 5 days after irradiation (days, $M \pm \sigma$)

	Vaccination doses		
Groups mice	3.2×10	3.2×10^2	3.2×10^3
Vaccination without irradiation	9.0 ± 0.6	7.0 ± 0.3	7.1 ± 0.7
Vaccination and irradiation in dose 1 Gy	8.6 ± 0.7	7.4 ± 0.5	6.9 ± 0.4
Vaccination and irradiation in dose 4 Gy	7.1 ± 0.9*	6.8 ± 0.6	6.3 ± 0.5

*$p < 0.05$

TABLE 2. Lifetime between inoculation of different doses of *F. tularensis* cells in 26 days following irradiation (4 Gy) and death of mice (days, $M \pm \sigma$).

Vaccination dose	Control (without irradiation)	Vaccination after irradiation in dose 4 Gy
1.5×10^4	6.9 ± 0.7	6.2 ± 0.6
1.5×10^3	6.9 ± 0.6	6.8 ± 0.7
1.5×10^2	7.8 ± 0.7	8.2 ± 0.3
1.5×10	8.6 ± 1.1	9.1 ± 1.4

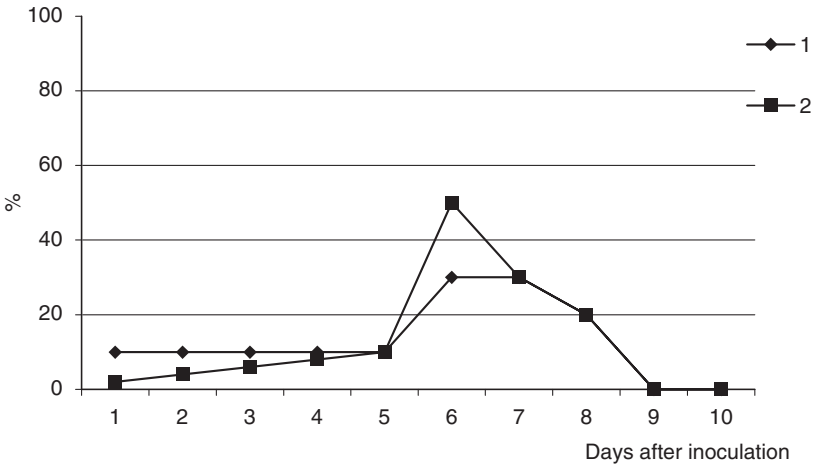

Fig. 4. Mortality of control and irradiated (4 Gy) mice after vaccination of 1.5×10^4 *F. tularensis* cells (%). 1−1.5×10^4; 2−4 Gy + 1.5×10^4

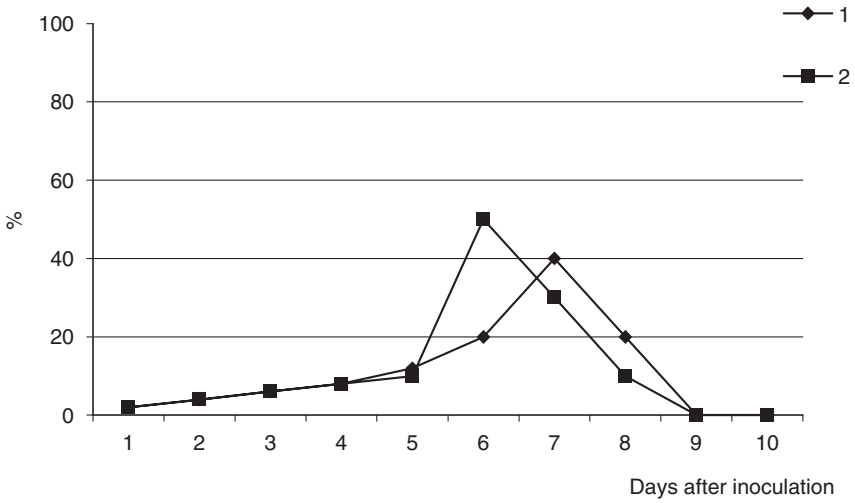

Fig. 5. Mortality of control and irradiated (4 Gy) mice after vaccination of 1.5×10^4 *F. tularensis* cells (%). 1−1.5×10^4; 2−4 Gy + 1.5×10^4

An absence of significant difference in the level of "residual virulence" (LD50) and time of death between irradiated and non-irradiated cells was registered. The data demonstrated an aggravation of vaccination process of *F. tularensis* at the initial stage of the development of radiation damage and insignificant difference between irradiated and non-irradiated mice during the recovery period of immunological resistance of the body.

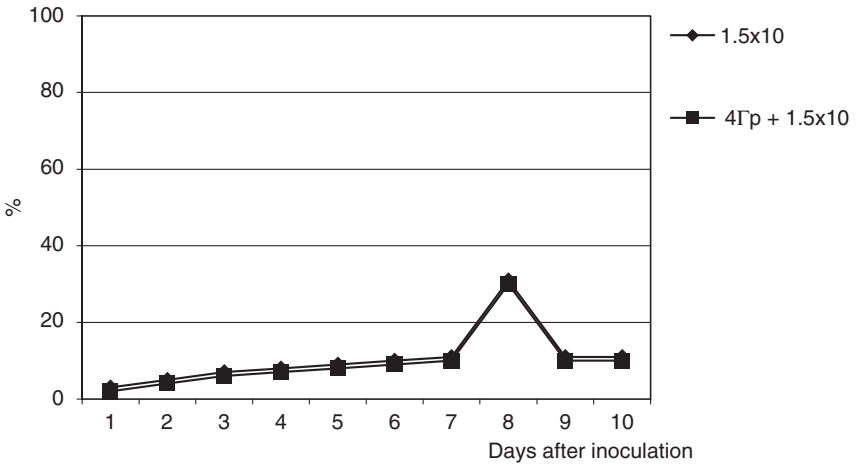

Fig. 6. Mortality of control and irradiated (4 Gy) mice after vaccination of 1.5×10 *F. tularensis* cells (%). 1−1.5×10; 2−4 Gy + 1.5×10

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