EFFECT OF BCG VACCINE ON THE OUTCOME OF IRRADIATION OF RATS WITH γ-RAYS FROM Co^{60}

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Experimental studies of vaccination against tuberculosis have shown that BCG vaccine not only increases the specific resistance of the organism to tuberculous infection, but also promotes reactivity. An increase in the nonspecific resistance to infection by pyogenic staphylococci [8] and paratyphoid bacteria [6], and increase in the intensity of transplantation immunity [5], an increase in the stabilizing function of certain physiological regulating systems [3], and stimulation of immunogenesis in irradiated and unirradiated animals [1] have all been reported.

Adminstration of BCG vaccine before irradiation has been found to increase the radioresistance of the animals [2, 4, 5].

Investigations have demonstrated the favorable effect of BCG vaccination on the development of transplantable tumors: the mortality among the animals is reduced, the incidence of metastasization falls, and in some cases regression and absorption of the tumor takes place [9-13].

Bearing in mind these results indicating the beneficial effect of BCG vaccine on the course of radiation injuries caused by external irradiation, it was decided to investigate the influence of this preparation on the late sequelae of irradiation by γ-rays from Co^{60}, manifested by the development of tumors in various organs of the experimental animals.

EXPERIMENTAL METHOD

Experiments were carried out on 250 female Wistar albino rats weighing from 130-150 g.

The BCG vaccine was prepared in the N. F. Gamaleya Institute and injected intradermally in a dose of 4 mg per rate, the same with all injections, made up in 0.2 ml physiological saline.

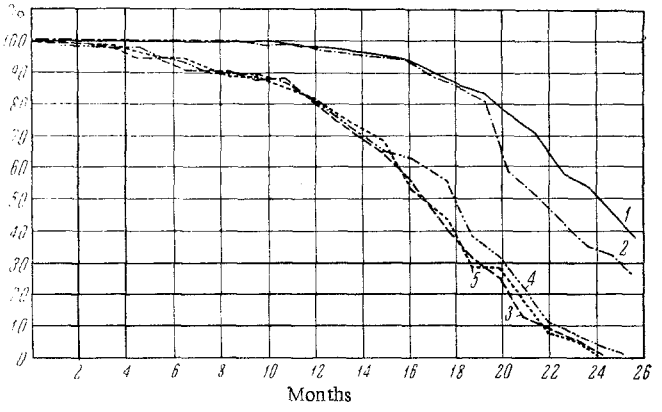

Fig. 1. Effect of vaccination on life span of control and irradiated rats. 1) Control (untreated); 2) vaccination; 3) irradiation; 4) irradiation + vaccination; 5) vaccination + irradiation.

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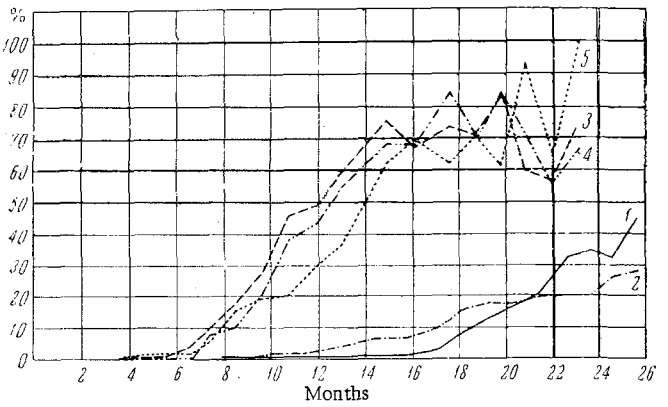

Fig. 2. Effect of vaccination on the time of appearance of mammary gland tumors in rats. Legend as in Fig. 1.

The rats were irradiated with γ-rays from a cobalt source (dose rate 236 R/min) in a single dose of 300 R. All the animals were subdivided into 5 groups. The rats of group 1 were irradiated in a dose of 300 R. The animals of group 2 were not irradiated and were vaccinated three times with intervals of three months between injections of the vaccine. The animals of group 3 were first irradiated and then vaccinated twice, three and six months after irradiation. The rats of group 4 were vaccinated two weeks before irradiation, and then again twice after irradiation by the same scheme of vaccination as the animals of group 2. The rats of group 5 received no treatment whatever and acted as controls. After injection of the BCG vaccine, slight induration of the skin of the rats was observed (without necrosis at the site of injection); this was absorbed during the next two weeks. All the animals were kept in the vivarium in identical conditions and on the same diet. The morphological composition of the blood (erythrocyte and leukocyte counts, leukocyte formula), the life span, and the speed and frequency of development of mammary gland tumors were studied in the control and experimental animals.

EXPERIMENTAL RESULTS

The changes in the erythrocyte count in the blood of the experimental animals were very slight and lay within normal limits. During the first month a slight decrease in the erythrocyte count was observed (by 10-18%), but later the erythrocyte count in the rats of all the groups was above the initial level.

The changes in the leukocytes were more marked. The total number of leukocytes in the irradiated rats fell by 60-80% in the first two weeks after irradiation. In the intact rats fluctuations within limits of ± 15-20% were observed, with a tendency toward a decrease in the later stages. In the vaccinated rats, both irradiated (groups 3 and 4) and unirradiated (group 2), the total leukocyte count was increased by 40-80% after each injection of vaccine. This change took place on account of an increase in the neutrophil count up to 275-560% of its initial value. The absolute lymphocyte count varied within limits of ± 20-30%, with a slight decrease in the second year of the animals' life.

The results of the experiment to determine the effect of BCG vaccination on the life span and incidence of mammary gland tumors in femal Wistar rats are shown in Figs. 1 and 2. It is clear from Fig. 1 that the rats irradiated with γ-rays from Co^{60} in a dose of 300 R died much quicker than the control animals. The life span of the control (group 5) and vaccinated (group 2) rats was practically identical. No. significant differences were found in the life span of the irradiated rats vaccinated before and after irradiation (groups 3 and 4, see Fig. 1).

It will be seen from Fig. 2 that the speed and frequency of development of mammary gland tumors in the irradiated rats (groups 1, 3, and 4) were much higher than in the intact (group 5) and vaccinated (group 2) animals. Vaccination of the rats before irradiation led to a slight decrease in the frequency of mammary gland tumors. The maximal incidence of mammary gland tumors in the irradiated rats was observed 15-20 months after irradiation (70-80%), and it was significantly higher than in the control rats (20-40%), and the tumors, moreover, were found sooner than in the control animals (22-26 months after irradiation).

The results of these experiments show that BCG vaccination, carried out before irradiation on animals, lowered the rate and incidence of development of mammary gland tumors. Vaccination given after

irradiation had no such effect (see Fig. 2). On the 325th, 360th, and 390th days after irradiation tumors were found in previously vaccinated animals in 20.6, 30.0, and 35.7% of cases respectively, and among the control irradiated rats in 45.5, 49.1, and 59% respectively. These differences are statistically significant. In the later stages the differences in incidence of the tumors were not significant or absent altogether. In the unirradiated, vaccinated rats, tumors appeared somewhat earlier than in the intact animals receiving no treatment whatever (Fig. 2). However, as statistical analysis using the χ^2 criterion showed, these differences were not significant and evidently reflect fluctuations in the incidence of this tumor in the control animals. It is noteworthy that in the later stages (22-26 months) the incidence of mammary gland tumors in the vaccinated animals was lower than in the control, intact rats. This difference is not statistically significant, but it correlates with the slower mortality of the control rats at these times. Evidently the longer life span of the animals (in the absence of exposure to the action of additional factors) may itself contribute to the increase in the incidence of mammary gland tumors in female rats.

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