CHANGE IN THE PROPERDIN LEVEL IN THE BLOOD OF NORMAL AND IRRADIATED ANIMALS UNDER THE INFLUENCE OF A MUCOPOLYSACCHARIDE PREPARATION FROM CATTLE SPLEEN

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N. M. Ivanova and A. S. Shitikova

Laboratory of Radiation Immunohematology (Head G. M. Murav'ev), Leningrad Institute of Blood Transfusion (Director—Docent A. D. Belyakov), Leningrad
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It is known that mucopolysaccharides obtained from the tissues of animals, like bacterial lipopolysaccharides, affect the properdin level of the blood and the natural resistance of animals; they are close to bacterial lipopolysaccharides in the force of their action. The rate of appearance, magnitude, and duration of the effect depend on the dose of the mucopolysaccharide preparation. The administration of relatively small doses of the preparation produces a rapid increase in the properdin level in normal animals, while large doses produce an initial decrease in the properdin titer, followed by an increase in it [5, 7]. Thus, different amounts of mucopolysaccharide in the organism differently affect the blood properdin level, and in view of this, the resistance of the organism as well.

In this work we investigated the effect of a mucopolysaccharide preparation obtained from cattle spleen on the blood properdin level of normal animals and after x-ray irradiation.

EXPERIMENTAL PROCEDURE

The preparation, consisting of a peptide and a polysaccharide, containing hexosamine and galactose, was produced under sterile conditions and chemically examined by coworkers of our laboratory, Z. P. Karmanova, E. I. Turchenko, and T. M. Ostroukhova. The hexosamine content was 13.2%, reducing sugars liberated after hydrolysis with one normal sulfuric acid 19%, and total nitrogen 7.6%. The preparation contains sialic acids, characteristic of neutral mucopolysaccharides, as well as a substantial amount of aspartic and glutamic acids. The experiments were conducted on white mice, 18-20 g in weight, and rabbits 2.5-3 kg in weight.

The preparations were injected intravenously in sterile physiologic solution in the following volumes: 0.2 ml per mouse and 1 ml per rabbit. The control animals received only physiologic solution. Doses of 0.5 and 0.3 mg per kg of weight of the rabbit and 0.5, 1, 2, and 4 mg per mouse were used to investigate the influence of the mucopolysaccharide preparation on the properdin level in normal animals. Blood samples were taken from the rabbits from the veins of the ear in a volume of 3 ml before injection of the preparation and on the first, third, fifth, seventh, and tenth days after the injection. A total of 22 rabbits were used in the experiments, nine of them serving as controls. Blood was taken from the mice at the same periods with a Pasteur pipette from the venous plexus of the eye. The mice were exsanguinated entirely, and blood was taken from six to ten mice on each day of the experiment to determine the properdin titer. A total of 250 mice were used in the experiments.

Doses of 0.5 mg per kg of weight of the rabbit two days before irradiation and 1 mg per mouse three days before irradiation were used to investigate the influence of preliminary injection of a mucopolysaccharide preparation on the blood properdin level of the irradiated animals. Irradiation was conducted on the RUM-3 apparatus under the following conditions: voltage 185 kV, current strength 15 mA, filter Cu 0.5 mm, distance for rabbits 40 cm, dose rate 44 R/min, dose 1000 R; distance 30 cm for mice, dose rate 77 R/min, dose 650 R. A total of 17 rabbits and 130 mice were irradiated.

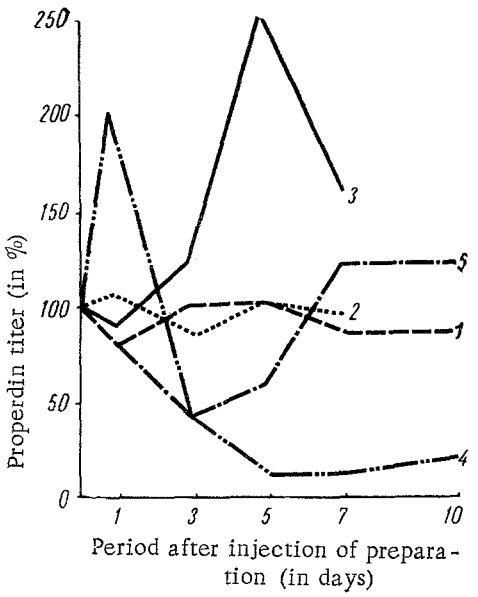

Fig. 1. Effect of various doses of mucopolysaccharides on the properdin titer in mice. 1) Control; 2) injection of preparation in a dose of 0.5 mg; 3) 1 mg; 4) 2 mg; 5) 4 mg of preparation per mouse.

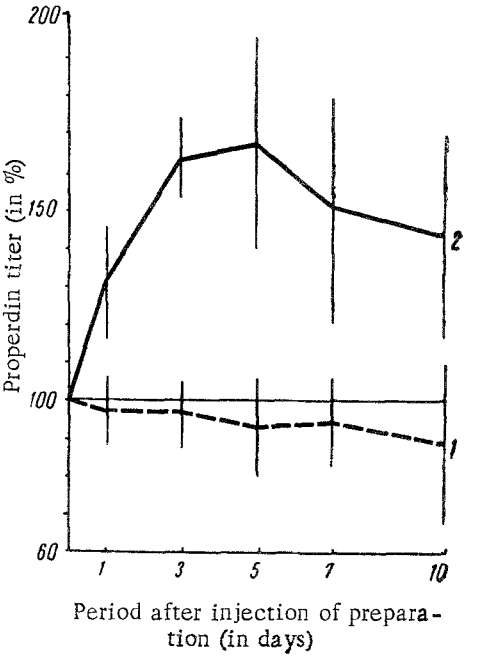

Fig. 2. Variation of properdin titer in rabbits after the injection of mucopolysaccharide preparation. 1) Control; 2) injection of 0.5 mg of the preparation. Vertical lines—standard deviations of the average values.

The properdin titer was determined in the intact animals and subsequently on the first, third, fifth, seventh, and tenth days after irradiation. For mice, the experiments were continued up to one month. In all the experiments the serum was kept at 27° before titration. The determination of the properdin titer was conducted according to the Rozental'-Savel'vol'f procedure [2]. Zymosan for titration of the properdin was produced according to Karmanova's method [1]. The data of the determinations are expressed in percent of the initial level.

RESULTS OF THE EXPERIMENTS

The most effective dose of the preparation was determined in the first group of experiments on mice. Figure 1 presents the dynamics of the properdin titer.

In the control group (physiologic solution), the fluctuations of the properdin level lay within the range 80-100%. The least dose (0.5 mg) proved ineffective. The greatest dose (4 mg) led to a decrease in the properdin titer that lasted until the fifth day. Such inhibition was also observed when a dose of 2 mg was used, but after a transitory rise on the first day. The most effective was a dose of 1 mg, at which the properdin level was increased by 150% by the fifth day, followed by some decrease by the seventh day after injection of the preparation.

In the rabbits (Fig. 2), no significant deviation of the properdin titer from the initial level was observed after the injection of physiologic solution. After the injection of 0.5 mg of the preparation per kg of weight, a regular stimulation of the properdin formation was observed in 11 out of 13 rabbits, beginning on the first day. In certain rabbits, a decrease in the properdin titer to 46-50% was observed on the first day. The maximum rise was observed on the third to fifth day after the injection and proved statistically reliable ($P < 0.05$-0.01). The maximum values of the properdin titer in individual rabbits comprised an average of 200%. The dose, equal to 0.3 mg per kg of weight, proved ineffective—only in one out of five rabbits was an increase in the properdin level to 320% noted.

There are indications that the infection of mice during the period of increased properdin level, as a result of the injection of tissue mucopolysaccharide preparations, gives a substantially lower death rate in comparison with with control animals [7].

In view of this, we irradiated mice on the third day after the injection of 1 mg of the test preparation, when the properdin titer was beginning to increase in comparison with the initial level. Rabbits were irradiated on the second day after the injection of 0.5 mg of the preparation, i.e., also during the period of the rise in the properdin level.

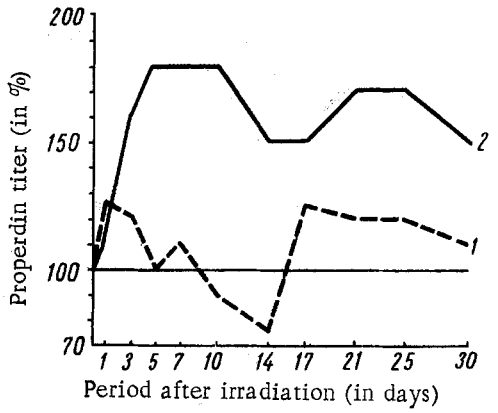

Fig. 3. Variation of the properdin titer in mice after x-ray irradiation. 1) Control; 2) after preliminary injection of 1 mg of mucopolysaccharide preparation.

As it follows from Fig. 3, after irradiation a transitory increase in the properdin titer was observed in the mice of the control group during the first days, later replaced by a decrease, with a maximum drop by the 14th day after irradiation. The properdin level subsequently increased, which coincided in time with the cessation of dying of the irradiated mice. In the group of mice with preliminary injection of 1 mg of the preparation, the properdin titer far exceeded the initial level and the fluctuations in the control group during the entire investigation period.

The properdin level in the blood of the irradiated animals, both in the control group and after preliminary injection of mucopolysaccharide preparation, varied substantially, which hindered their expression in the form of average quantities. An analysis of the data of each experiment showed that after irradiation, in five out of nine cases a decrease in the properdin level, up to 50% on the average, was observed in the control rabbits after irradiation. In the remaining four rabbits, the properdin level was unchanged or was increased an average of up to 129% by the fifth day, but subsequently again decreased by the seventh to tenth day. In the experimental group, only in two out of seven rabbits was a uniform decrease in the properdin titer observed from the first to third day; the level decreased to a lesser degree than in the corresponding control group. In the five remaining experimental rabbits, the properdin level was unchanged or even increased by the fifth day to an average of 145%, remaining within the limits of the initial level on the seventh to tenth days.

The experiments on irradiated rabbits were conducted with a small number of animals; hence, their results were less distinct. However, they confirm the stimulating effect of preliminary injection of the mucopolysaccharide preparation on the properdin level, which was demonstrated with sufficient clarity in the experiments on mice. The positive effect is probably due to an increase in the properdin level by the moment of irradiation as a result of the preliminary injection of the preparation.

There are indications that mucopolysaccharides that exhibit the described influence on the properdin system may also be formed endogenously. It is believed that endogenous mucopolysaccharides are formed in small amounts after the injection of bacterial lipopolysaccharides and are responsible for the stimulating effect on the properdin level [5]. In a number of pathological states accompanied by tissue decomposition (radiation sickness, tuberculosis, malignant neoplasms, hemorrhagic shock, posttraumatic inflammation), endogenous mucopolysaccharides may be formed in amounts toxic to the organism [4-8]. In these cases properdin ties up the excess endotoxin-like mucopolysaccharides and thereby protects the organism from their toxic action. Hence, preliminary activation of the properdin system by small doses of mucopolysaccharide substances or bacterial lipopolysaccharides may be favorable in certain severe injuries, accompanied by a decrease in the natural resistance of the organism and by the formation of large amounts of endogenous mucopolysaccharides, as is the case in radiation sickness [3].

Actually, in our experiments we observed a statistically reliable increase in the survival of the mice when they were irradiated during the period of increasing properdin content, as a result of the injection of an effective dose of the mucopolysaccharide preparation. The experiments were conducted on 160 mice (half of them controls) under the same conditions of prophylactic injection of the preparation and irradiation as in the experiments on the determination of the properdin content. The survival for 30 days comprised 27.5% in the control group of animals, and 46.3% in the experimental group ($P < 0.02$).

Thus, the prophylactic administration of small doses of a mucopolysaccharide preparation from cattle spleen results in an increased properdin level in the blood and has a favorable effect upon the survival of irradiated animals.

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