

EFFECT OF MICROBIAL POLYSACCHARIDES ON THE FUNCTIONAL STATE OF THE RETICULO ENDOTHELIAL SYSTEM IN ALBINO MICE

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Polysaccharide preparations from yeast-like fungi and actinomycetes, when injected parenterally into animals 1-7 days before the experiment, stimulated the phagocytic activity of cells of the reticuloendothelial system (RES) and led to an increase in weight of the liver and spleen. The purified polysaccharides (glucans and mannan) had a less marked action. The increase in phagocytic activity of the RES corresponded to the period of resistance of the albino mice to staphylococcal septicemia.

Polysaccharide preparations from some yeast-like organisms and actinomycetes, when injected parenterally into animals, cause an increase in the nonspecific resistance of the recipient to various types of unfavorable factors, such as bacterial and virus infections, poisoning, irradiation, and so on [1, 5, 6, 14]. To a certain degree the increase in nonspecific resistance depends on the functional activity of the reticuloendothelial system (RES). The effects of some bacterial polysaccharides and endotoxins on RES function have been investigated [3, 4, 7-9, 11, 12]. All workers report the biphasic character of the response of the macrophagal system: a decrease in its activity during the first hours after injection of the polysaccharides followed by stimulation of phagocytic activity of the RES.

However, no investigations into the effect of polysaccharide preparations from actinomycetes or yeast-like fungi on the phagocytic function of the RES in animals could be found in the accessible literature.

In the investigation described below the role and the degree of participation of the RES in the mechanism of the biological activity of microbial polysaccharides were studied.

EXPERIMENTAL METHOD

Polysaccharide preparations, both as complexes and purified (glucan and mannan), were selected as follows for the experiments: C₃ - phosphoamino-polysaccharide-peptide complex containing 40% reducing substances (from *Actinomyces coelicolor*); 1E - a gluco-mannan containing 52% of reducing substances (from *Candida albicans*); 6E - a gluco-galactan containing 48.5% of reducing substances (from *Rh. glutinis*); 6E_{II} - a glucan containing 65% of reducing substances (from *Rh. glutinis*); 11_{gl} - a glucan containing 89% of reducing substances (from *A. pullulans*); 55E - a mannan containing 88% of reducing substances (from *C. tropicalis*).

The polysaccharides were injected intraperitoneally in a dose of 200-500 µg per mouse 1-2 h and 1, 3, 7, 15, and 30 days before the experiment. Noninbred albino mice weighing 18-20 g were used in a total number of 500. The phagocytic activity of the RES was studied by the method of Halpern et al. [13], based on the periodic determination of the rate of disappearance of foreign nucleated erythrocytes from the

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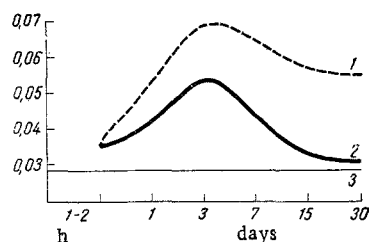


Fig. 1

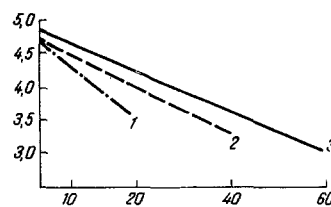


Fig. 2

Fig. 1. Changes in phagocytic index (K) after injection of polysaccharides: 1) complex polysaccharides; 2) purified polysaccharides; 3) control. Abscissa, time of injection of polysaccharides before experiment; ordinate, phagocytic index K.

Fig. 2. Elimination of pigeon's erythrocytes from blood of mice after injections of polysaccharides (1-3 days after injection of polysaccharides): 1) complex polysaccharides; 2) purified polysaccharides; 3) control. Abscissa, time of determination of phagocytic activity of RES (in min); ordinate, log of number of pigeon's erythrocytes per mm^3 mouse blood.

blood of the mice. Pigeon's erythrocytes were injected intravenously in a dose of 200,000 cells per mouse together with heparin to prevent thrombus formation in the vessels. The rate of clearance of the blood from pigeon erythrocytes was measured by taking blood samples (0.05 ml) from the retro-orbital venous plexus at fixed time intervals for 1 h. At the end of the experiment the mice were sacrificed and the liver and spleen were removed and weighed.

EXPERIMENTAL RESULTS

During the first hours after injection of the polysaccharides no change was found in the phagocytic activity of the macrophages. The rate of disappearance of the foreign erythrocytes from the blood of the experimental animals was the same as in the control group.

Subsequently from 1-7 days after single injections of the polysaccharide preparations an increase in the phagocytic activity of the RES cells could be observed. Irrespective of the source from which the polysaccharides were obtained and also of the dose of the preparations, a marked stimulating effect on RES function was noted. This state persisted within certain limits throughout the experiment (Fig. 1).

However, after injection of the purified polysaccharides (glucans 6EII and 11gI or mannan 55E) into the mice the rate of phagocytosis of the RES cells was reduced and the index K was lowered. If the polysaccharides were injected 15 and 30 h before the experiment, the values of the phagocytic index were almost identical with those in the control. This can evidently be attributed to the fact that the purified polysaccharides are metabolized more rapidly and thus removed from the blood stream.

As the results of these experiments show, a study of the rate of removal of pigeon erythrocytes from the blood of the mice after injection of the polysaccharide preparations showed that most nucleated cells disappeared from the blood stream within 20 min, whereas in the animals of the control group of animals foreign erythrocytes could still be found 1 h after injection in numbers of between 1,500 and 2,000 (Fig. 2).

Stimulation of the phagocytic activity of the RES corresponds to the period of resistance of the mice to staphylococcal septicemia [1].

Preliminary injection of polysaccharide preparations from yeast-like organisms or actinomycetes thus help to increase the phagocytic activity of the RES cells. No period of inhibition of function of the macrophage system was observed during the first few hours after injection of the preparations, as is seen when bacterial lipopolysaccharides are administered to animals.

The high molecular weight of the endotoxins may perhaps facilitate their phagocytosis by RES cells, resulting in damage to those cells, with consequent decrease in the ability of the macrophages of the liver and spleen to remove foreign substances from the blood stream during the first few hours.

As these experiments showed, parenteral injection of polysaccharide preparations into mice causes an increase in the weight of organs richly supplied with reticulo endothelial cells [2]. However, the gradual increase in the weight of the liver and spleen toward the 3rd-5th days was clearly expressed only after injection of the polysaccharide complexes, whereas the purified polysaccharides had no such action. The stimulating effect on the weight of the animals' organs was probably due to intensification of proliferation in the RES, just as after administration of bacterial polysaccharides [8, 10-12, 15].

These results show that polysaccharides from yeast-like fungi and actinomycetes, after preliminary injection into animals, increase the functional activity of the RES.

This fact may play an important role in pathological states in which the processes of phagocytosis act as an important cellular factor of immunity.

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