

## PHARMACOLOGY OF PYROGENIC BACTERIAL POLYSACCHARIDES

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Pyrogenic polysaccharides obtained in a number of foreign laboratories are known to possess many-sided action on a whole series of organs and systems of both the healthy and diseased organism.

It has been shown in papers published by foreign authors that under the influence of "pyromene" (protein-free pyrogenic bacterial preparation, freed from anaphylactic properties) reparative processes undergo changes (Windl and Chambers [5]), vascular permeability is decreased (L. Greene [3]), leucocytosis sets in (D. Hankel, R. Mefferd, J. Loefer [2]), allergic states are abolished (Randolph and Rollins [4]).

There is no doubt that the properties of pyrogenic preparations have not yet been fully discovered. Nonetheless, those properties which are already known present great interest both for experimental and for clinical medicine.

A preparation of a pyrogenic polysaccharide has been obtained in Professor M. V. Svyatukhin's laboratory from a culture of *Proteus vulgaris*,\* and this preparation has been the material used in this work.

### EXPERIMENTAL METHODS

The general action and toxicity of the preparation were studied on sexually mature white mice weighing 20 g ( $\pm 2$  g). The preparation was given intraperitoneally (in solution), starting with 10  $\gamma$  and up to 5000  $\gamma$  per 1 kg body weight. Within this range of doses no changes, apart from some mild depression, were noted in the general state and behavior of the animals. Large doses could not be tried owing to the low solubility of the preparation.

Application of the polysaccharide to the mucosa and its subcutaneous and intramuscular injection revealed no locally irritating action.

### EXPERIMENTAL RESULTS

The pyrogenic action of the preparation, injected intravenously or intraperitoneally, is observed in rats, rabbits and dogs when doses as small as 1-2  $\gamma$  per kg are given. Of all the animals studied the least marked pyrogenic effect was observed in rats. Increasing the dose 10, 100 fold and more does not lead to pronounced enhancement of the pyrogenic effect, i.e., no clear correlation is seen between the pyrogenic effect and the dose of the preparation. The rise in temperature began, as a rule, within the first half-hour after injection and the temperature continued to rise in the course of 1  $\frac{1}{2}$  - 2  $\frac{1}{2}$  hours. The body temperature then began to decline reaching the initial level by the 5th - 7th hour.

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\* The method of preparation is described in the paper by A. A. Bodareva and M. V. Svyatukhin.

It is known that preliminary intravenous injection of novocaine (in rabbits and dogs) leads to delay in the rise of temperature amounting to 1½ to 2 hours and decreases the extent to which it rises (Fig. 1). Analogous effects were seen in rats under urethane anesthesia. Taking into account the available facts, it may be postulated that hyperthermia arising under the influence of pyrogenic polysaccharide is reflex in nature. It would appear that the reflex arising from vascular receptors is completed by way of the higher thermoregulatory centers. Anti-inflammatory properties of the pyrogenic polysaccharide were studied on rabbits using the technique described by I. A. Oivin and K. N. Monakova [1].

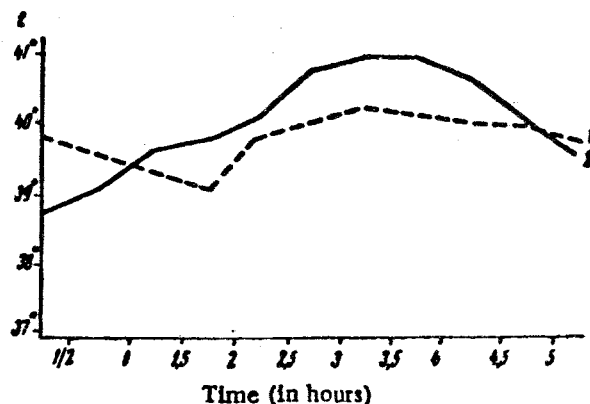


Fig. 1. Temperature reaction in novocaine-treated (1) and untreated (2) dog.

The results of the experiments indicate that under the influence of the preparation a gradual slowing of escape of dye-stuff from the vessels takes place (Fig. 2), i.e., the preparation possesses some slight anti-inflammatory properties.

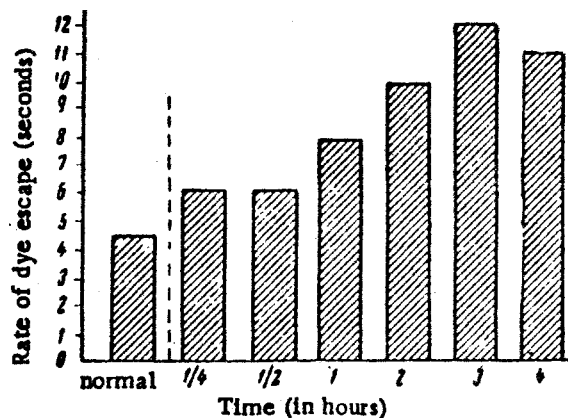


Fig. 2. The rate (in seconds) of escape of dye-stuff from capillaries at different intervals following administration of pyrogenic polysaccharide.

The influence of the bacterial polysaccharide on arterial blood pressure and respiration was studied in acute experiments on nonnarcotized rabbits and dogs under morphine-urethane anesthesia. In these experiments it was found that if intravenous injection of the preparation started with small doses (2-20 γ per kg) then no substantial changes in blood pressure, rate of cardiac contractions and nature of respiration were observed.

even if the dose was then sharply increased (500  $\gamma$  per kg); but if doses of 500  $\gamma$  per kg and over were given at the very beginning of the experiment a transient fall in blood pressure and depression of respiration down to apnea were observed upon the first injection (Fig. 3). All subsequent injections of the preparation in the same animal do not elicit the same effect even when large doses (1000-2000  $\gamma$  per kg) are given.

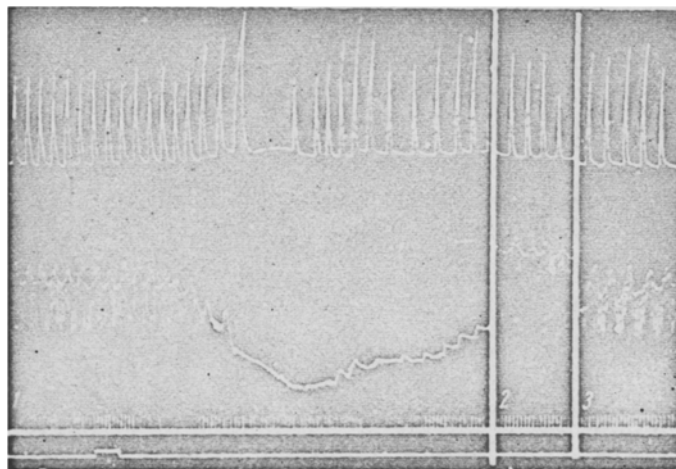


Fig. 3. The effect of a large dose (500  $\gamma$  per kg) of pyrogenic polysaccharide on arterial blood pressure and respiration upon being injected for the first time.

Records from above down: respiration, blood pressure in the femoral artery, time marker (1 second), injection of preparation. 1) Normal and immediately after injection of preparation; 2) 5 minutes after injection; 3) 10 minutes after injection.

The bacterial polysaccharide in concentrations of 1:50,000 - 1:500 exerts no appreciable effect on the isolated frog heart (Straub method).

The effect on diuresis was studied in experiments on white rats weighing 170-200 g. The preparation was given intraperitoneally and "hydration" (5 ml boiled water per 100 g body weight) was carried out by introducing the water into the stomach. Observations over a period of 5 hours with recording every half hour did not reveal any noticeable difference in diuresis between the control and experimental animals.

The experiments performed may be summarized as follows.

Parenteral administration of the bacterial polysaccharide obtained from *Proteus vulgaris* cultures elicits a rise of body temperature in rats, rabbits and dogs when given in doses of 1  $\gamma$  per kg and larger. This rise in temperature continues for 5-7 hours. Preliminary treatment with novocaine or narcotization of the animals produces a delay in the rise of body temperature and diminishes the degree of such rise. Administration of the pyrogenic preparation is associated with decreased permeability of the blood vessels, i.e., the preparation exhibits some anti-inflammatory properties. Small doses of the preparation (2-20  $\gamma$  per kg) do not affect respiration and blood pressure appreciably; large doses (500  $\gamma$  per kg and over) elicit transient lowering of blood pressure and depression of respiration. The latter effect occurs only upon the first injection of the preparation. The pyrogenic polysaccharide preparation under investigation is of low toxicity.

## SUMMARY

Certain aspects of the pharmacodynamics of bacterial pyrogenic polysaccharides were studied in this work. It was established that there is an increase of the body temperature in animals, which lasts for 6-7 hours, following parenteral administration of this preparation in the dose from 1γ per kilogram and over. Preliminary administration of novocaine and anesthesia to these animals causes delay in the rise of body temperature and decreases the degree of its rise. The preparation has mild anti-inflammatory properties and its toxicity is low. It has no effect on respiration and blood pressure in the doses of 2-20 γ per kilogram of body weight. There is no disturbance of diuresis following administration of this preparation.

## LITERATURE CITED

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