EFFECT OF PYROGENAL ON ADRENAL CORTICAL FUNCTION

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Pyrogenal is a lipo-polysaccharide complex from gram-negative bacteria [1, 2]. Besides an increase of body temperature it causes several other response reactions of the macroorganism: it alters the capillary permeability [3], depresses the development of anaphylactic shock and the Arthus' phenomenon [5, 6], and inhibits scar formation [4, 7]. It may be supposed that these aspects of the activity of pyrogenal are associated with its power of stimulating the hypophyso-adrenal system.

Studies were made of the effect of pyrogenal on the adrenal cortical function, using as test the determination of the concentration of free 17-hydroxycorticosteroids in the plasma of the circulating blood.

EXPERIMENTAL METHOD

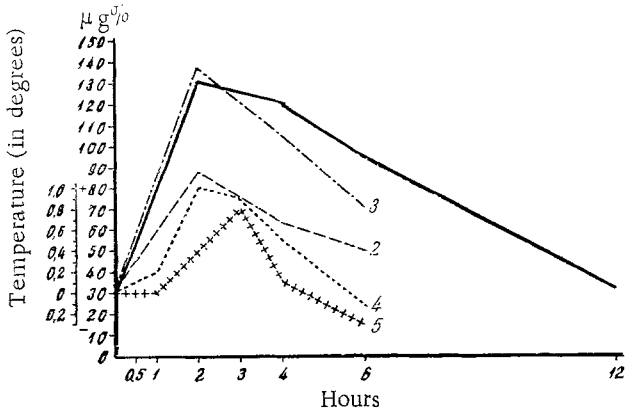
Experiments were carried out on male guinea pigs weighing 300-350 g. The animals of the experimental groups received an intraperitoneal injection of pyrogenal solution and the control animals a corresponding injection of physiological saline. Blood was taken from the animals by cardiac puncture. The concentration of free 17-hydrocorticosteroids was determined in 1 ml of plasma by the method of Silber and Porter, as modified by Yudaev and Pankov [8]. The body temperature was measured by means of a mercury maximum thermometer inserted into the rectum to a depth of 3 cm.

EXPERIMENTAL RESULTS

Thirty min after injection of pyrogenal in a dose of 10 μg/kg into the guinea pigs a nonspecific increase in the concentration of corticosteroids was observed, and a similar reaction was noted in the control animals (see figure). Two hours after the injection the concentration of 17-hydroxycorticosteroids in the plasma of the control animals fell to the initial level, whereas in the experimental animals a further increase in the concentration was observed to 131.5 μg%, or more than 3.9 times greater than its initial value. After an interval of 4 h the concentration of corticosteroids in the plasma of the guinea pigs receiving pyrogenal remained at the same level, after 6 h it fell to 94.9 μg%, and 12 h after injection of the preparation it returned to its original level. The increase in the concentration of 17-hydroxycorticosteroids developing after injection of pyrogenal in a dose of 10 μg/kg corresponded in magnitude and duration to the changes produced in guinea pigs by an intraperitoneal injection of ACTH in a dose of 5 units/kg (see figure).

Comparison of the mean values of the change in body temperature and the concentration of 17-hydroxycorticosteroids (see figure) shows that these two reactions followed a parallel course, although the body temperature returned to its original level slightly sooner, i.e., after 5-6 h.

A single intraperitoneal injection of pyrogenal in a dose of 0.1 μg/kg did not lead to an increase in the concentration of corticosteroids or to a rise of temperature.



Concentration of 17-hydroxycorticosteroids in blood plasma of guinea pigs after a single (1) and repeated (2) injections of pyrogenal in a dose of 10 μg/kg and after injection of ACTH in a dose of 5 units/kg (3), and body temperature of animals after a single (4) and repeated (5) injections of pyrogenal in a dose of 10 μg/kg.

In the animals receiving pyrogenal in a dose of 10 μg/kg for a period of 7-8 days the corticosteroid level determined after the last injection of the preparation also was raised, although the increase was smaller than that arising after a single injection of pyrogenal, amounting to 52-67% of the latter. Hence, the phenomenon of tolerance may also extend to this aspect of the activity of the bacterial lipopolysaccharides. The temperature reaction in these animals also was smaller in height and duration (see figure).

Hence, pyrogenal, like other bacterial lipopolysaccharides [9, 13], stimulates the hypophyso-adrenal system, leading to an increase in the concentration of free 17-hydroxycorticosteroids in the circulating blood, and this may be of definite importance in the mechanism of action of this preparation on the host organism. The problem of the relationship between the temperature reaction and the change in the blood corticosteroid concentration requires further investigation.

SUMMARY

Along with a rise of the body temperature, intraperitoneal injection of pyrogenal into guinea pigs (10 μg/kg) led to a rise of the free 17-hydroxycorticosteroid concentration in the peripheral blood plasma with the daily administration of pyrogenal for 7 to 8 days, there was a reduction both of the temperature reaction and of the degree of increase of the 17-hydroxycorticosteroid.

LITERATURE CITED

1. P. Z. Budnitskaya, Pat. fiziol. 5, 69 (1960).
2. P. Z. Budnitskaya, Byull. éksper. biol. 3, 53 (1962).
3. E. N. Iordanskaya and T. N. Nesmeyanova, In book: Experimental Investigations and Clinical Application of Pyrogenal [in Russian], p. 34, Moscow (1961).
4. T. N. Nesmeyanova et al. In book: Experimental Investigations and Clinical Application of Pyrogenal [in Russian], p. 54. Moscow (1961).
5. N. A. Ozeretskovskii, In book: Experimental Investigations and Clinical Application of Pyrogenal [in Russian], p. 41, Moscow (1961).
6. E. V. Patskikh, In book: Experimental Investigations and Clinical Application of Pyrogenal [in Russian], p. 234. Moscow (1961).
7. L. V. Polezhaev et al. In book: Experimental Investigations and Clinical Application of Pyrogenal [in Russian], p. 74, Moscow (1961).
8. N. A. Yudaev and Yu. A. Pankov, Probl. éndokrinol, 2, 35 (1958).
9. N. Christy et al. Proc. Soc. exp. Biol. (N. Y.) (1956)., v. 91, p. 453.
10. R. Egdahl, J. clin. Invest (1959), v. 38, p. 1120.
11. R. Egdahl, et al., Proc. Soc. exp. Biol. (N. Y.) (1959), v. 101, p. 369.
12. R. Jones, et al., Endocrinology (1958), v. 62, p. 843.
13. J. Melby et al., J. Lab. clin. Med. (1960), v. 56, p. 50.