

## SOME ASPECTS OF THE ACTION OF THE SERUM OF FEBRILE ANIMALS

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O. Sh. Dzheksenbaev

Division of Infectious Pathology and Experimental Therapy of Infections  
(Head, Corresponding Member AMN SSSR Professor Kh. Kh. Planel'es), N. F. Gamaleya  
Institute of Epidemiology and Microbiology (Director, Professor P. A. Vershilova)  
of the AMN SSSR, Moscow (Presented by Active Member AMN SSSR P. F. Zdrodovskii)  
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It was shown by a previous investigation that the injection of a bacterial polysaccharide (pyrogenal) into guinea pigs causes, besides a rise of body temperature, an increase in the concentration of 17-hydroxycorticosteroids in the blood plasma [1]. No explanation of the interrelationship between these two processes has yet been suggested. At the present time great importance in the pathogenesis of various febrile reactions is attached to secondary endogenous pyrogenic substances appearing in the blood of animals whose body temperature is elevated, either after injection of bacterial lipopolysaccharides or during the development of certain infectious processes [2,4]. The chemical nature and biological importance of these substances have received incomplete study.

We have investigated the effect of the secondary endogenous pyrogenic substances on the level of the corticosteroids in the blood plasma of guinea pigs. There is no published work on this problem.

### EXPERIMENTAL METHOD

Experiments were conducted on male guinea pigs weighing 250-350 g during the autumn and winter. Endogenous pyrogens were obtained as follows. Pyrogenal was injected into the heart in a dose of 10  $\mu$ g/kg (in a volume of 1 ml). Two hours later, the body temperature of the animals was measured, and then they were totally exsanguinated from the heart. Next day, the sera obtained from the individual guinea pigs were pooled, centrifuged, and placed in the refrigerator. Preliminary seedings were performed to determine sterility. Instead of pyrogenal, the control group of animals received an injection of 1 ml of apyrogenic physiological saline. To prevent bacterial and pyrogenic contamination, the syringes, test tubes, and other vessels were subjected to dry heat for 2 h at 170°.

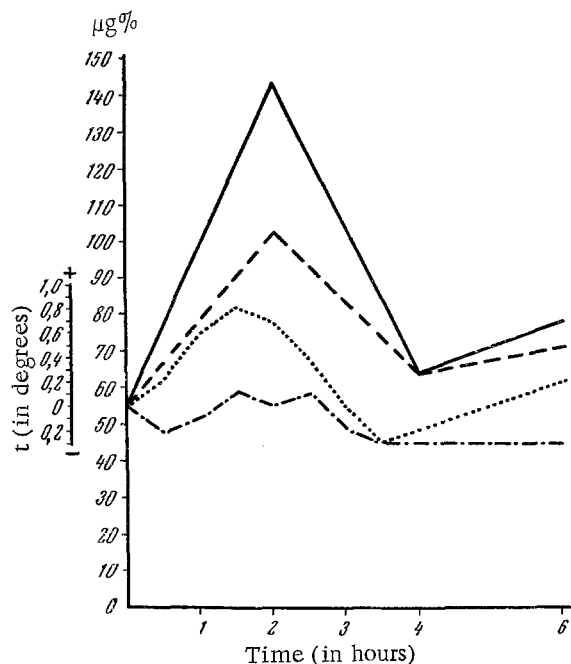
The free 17-hydroxycorticosteroids were determined in 1 ml of plasma by Silber and Porter's method as modified by Yudaev and Pankov [3]. Blood was taken from the animals by cardiac puncture 2, 4, and 6 h after injection of the serum. Both experimental and control groups of guinea pigs were used for each period. Blood was taken in the vivarium at a strictly definite time. To obtain plasma, the blood was placed in test tubes containing heparin in a dose of 20 units/ml of blood.

The body temperature was measured with a mercury maximum thermometer inserted into the rectum to a depth of 3 cm, at intervals of 30 min during the first 4 h and again 6 h after injection of the serum. The results were treated by statistical analysis using the "t" test. The differences were regarded as significant when  $P < 0.05$ .

### EXPERIMENTAL RESULTS

The injection of pyrogenal into guinea pigs was followed after 2 h by a rise of 1° in the body temperature. In the animals of the control group, which received injections of apyrogenic physiological saline instead of pyrogenal, the body temperature remained within the limits of its original level.

The serum containing endogenous pyrogenic substances, injected into the recipient guinea pigs, caused a short, monophasic increase in the body temperature (by 0.6-0.8°); an action of this type is characteristic of this group of substances (see figure). Injection of the serum of animals receiving physiological saline instead of pyrogenal, on the other hand, did not alter the body temperature which remained within the limits of its original level.



Influence of serum of febrile animals on level of 17-hydroxycorticosteroids in blood plasma and body temperature of guinea pigs. 1) concentration of hormones after injection of serum of febrile animals; 2) concentration of hormones after injection of serum of control animals; 3) body temperature after injection of serum of febrile animals; 4) body temperature after injection of serum of control animals.

original level. The change in the level of 17-hydroxycorticosteroids and in the body temperature in the two groups receiving serum containing endogenous pyrogens was identical.

Since the increase in the corticosteroid level after administration of pyrogenal may have taken place on account of the secretion of endogenous ACTH, it is quite possible that the observed stimulant action of the serum containing endogenous pyrogens was associated with the transfer of this hormone and of the corticosteroids themselves.

It is clear from the figure and table that injection of the serum obtained from the control animals led, after the lapse of 2 h, to an increase of 86% in the corticosteroid level over its initial value. This increase, however, should be regarded as a nonspecific reaction to this method of injection, for the intracardial injection of physiological saline in the same volume led to a similar increase in the concentration of 17-hydroxycorticosteroids. The corticosteroid level fell to its initial value after 4 h. In the group of recipient guinea pigs receiving serum containing endogenous pyrogens, the increase in the concentration of hormones after 2 h amounted to more than 158% of the initial level and to 39% of the level in the control group ( $P < 0.001$ ). After 4 h the hormone concentration fell to its initial level.

To exclude the possibility that remnants of the bacterial lipopolysaccharides circulating in the donors' blood may have acted on the hypophysis-adrenal system, experiments were conducted in which the same serum, containing endogenous pyrogens, was injected into a group of normal guinea pigs and a group of animals which had become accustomed to pyrogenal as a result of daily intraperitoneal injection of the substance in a dose of 10 µg/kg for 7 days. The maximal deviation of the body temperature from its initial level at the first injection of the preparation was 0.9°, and at the seventh -0.3°. Consequently, a significant degree of habituation was obtained, for the body temperature in this group of guinea pigs in fact remained within the limits of its

Effect of Serum of Febrile Animals on Concentration of Free 17-Hydroxycorticosteroids in Blood Plasma of Guinea Pigs

Group of Animals	Concentration of 17-hydroxycorticosteroids (in µg %)			
	Initial	After injection of Serum		
		After 2 h	After 4 h	After 6 h
Experimental . . . . .	55.6 ± 6.3 (17) *	143.3 ± 9.4 (24)	64.3 ± 4.5 (13)	78.1 ± 8.5 (14)
Control . . . . .		103.1 ± 7.3 (22)	64.1 ± 9.9 (13)	71.0 ± 6.3 (13)
P . . . . .	—	<0.001	>0.05	>0.05

\*The number of animals in which the hormone concentration was determined is shown in parentheses.

To exclude this possibility the following experiment was performed. ACTH was injected intraperitoneally in a dose of 10 units/kg, and 2 h later blood was withdrawn by cardiac puncture. The serum thus obtained caused the same increase in the concentration of 17-hydroxycorticosteroids and the same absence of changes in the body temperature as the serum of the animals of the control group. Consequently, the injection of serum containing endogenous pyrogens, besides causing a rise of body temperature, caused a transient increase in the concentration of 17-hydroxycorticosteroids in the peripheral blood of guinea pigs. This property of the serum of febrile animals was not connected with the presence of bacterial polysaccharides or ACTH.

#### LITERATURE CITED

1. O. Sh. Dzheksenbaev and N. A. Ozeretskovskii, Byull. éksper. biol., 5, 31 (1964).
2. O. Sh. Dzheksenbaev, In book: Experimental Investigations and Clinical Application of Pyrogenal [in Russian], (1961), p. 24.
3. N. A. Yudaev and Yu. A. Pankov, Probl. éndokrinol., 2, 35 (1958).
4. E. Atkins, Physiol. Rev., 40, (1960), p. 580.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.