FORMATION OF AN ENDOGENOUS PYROGEN IN NORMAL AND THYROIDECTOMIZED RABBITS

UDC 612.445 : 612.57

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 57, No. 4, pp. 49-51, April, 1964
Original article submitted April 2, 1963

In the pathogenesis of febrile states of different etiology, considerable importance is attached to an endogenous pyrogenic substance appearing in the blood of animals and man when the body temperature is raised after injection of bacterial polysaccharides or as a result of the development of certain infectious and allergic processes [2, 4]. The chemical properties, the biological action, and also the role of this substance in the development of the habituation (not the immunological tolerance) appearing after repeated injection of bacterial endotoxins have received inadequate study. In a previous paper we described results showing the thyroidectomy depresses the febrile reaction created by injection of the bacterial lipopolysaccharide "pyrogenal" [1].

The object of the present investigation was to study the role of endogenous pyrogen in the development of the fever produced by pyrogenal in normal and thyroidectomized rabbits. A special series of experiments was conducted on animals in which a state of habituation to the preparation had been created.

EXPERIMENTAL METHOD

Experiments were carried out on male chinchilla rabbits weighing 2.5-3.5 kg. Engodenous pyrogen was obtained by the method of Atkins and Wood [3], 2 h after administration of pyrogenal. The dose of the preparation was 2.5 μg/kg, and the volume of serum, containing endogenous pyrogen, injected into the recipients was 10 ml/kg. A state of habituation was created by intravenous injection of pyrogenal daily for 7 days in the usual dose of 2.5 μg/kg. The technique of thyroidectomy, and the method of calculating the febrile index from the increase of rectal temperature were similar to those described previously [1], with the exception that the intervals between the measurements of the body temperature were shortened to 30 min. The animals were used in the experiments 20-40 days after the operation. The numerical results were subjected to statistical analysis.

EXPERIMENTSL RESULTS

In 47 of 52 cases injection of serum from animals with pyrexia following administration of pyrogenal into recipient rabbits caused a febrile reaction, i.e., endogenous pyrogen was found in the recipients (see table). The presence of this substance in the serum was revealed by a short monophasic rise of the body temperature by 0.6-1.0° for 3 h and by the development of the same temperature reaction in the rabbits tolerant to pyrogenal.

It will be clear from the results given in the table that in 41% of cases no endogenous pyrogen could be could in the sera of the animals of this group; in 10% of normal rabbits it was likewise absent ($P < 0.01$).

Another series of experiments was carried out to determine endogenous pyrogen in the blood of normal and thyroidectomized rabbits after daily injection of pyrogenal into the animals for 7 days. In normal rabbits the febrile reaction to the 1st injection of the preparation amounted to 139 conventional units, and that to the 7th injection was 73 conventional units ($P < 0.01$). Endogenous pyrogen was found on the 7th day in 2 of the 12 rabbits included in the

Demonstration of Endogenous Pyrogen in the Blood of Normal and Thyroidectomized Rabbits

Group of rabbits	Number of animals			P
	total	with presence of pyrogen	with absence of pyrogen	
Normal	52	47	5	
Thyroidectomized	32	19	13	< 0.01

experiments (in normal intolerant animals endogenous pyrogen was found in 47 of 52 cases; comparison by the X^2 method gives $P < 0.01$).

No lowering the febrile reaction was observed in the thyroidectomized rabbits after repeated injections of pyrogenal. After the 1st injection the increase of body temperature was 63 conventional units, and after the 7th injection – 87 conventional units ($P > 0.05$). The frequency with which endogenous pyrogen was found in this group of animals was not lowered (in the thyroidectomized, intolerant rabbits endogenous pyrogen was found in 19 of 32 cases, in the tolerant animals in 3 of 12 cases; $P > 0.05$).

The reduction of the pyrogenal fever in the rabbits after thyroidectomy might be due to a lowering of the sensitivity of the thermoregulatory centers to the action of endogenous pyrogen, and experiments were accordingly carried out in which normal and thyroidectomized animals were injected with the same serum containing endogenous pyrogen. No difference was found between the febrile indices of the two groups of rabbits (in the normal animals – 53 conventional units, and in the thyroidectomized rabbits – 56 conventional units; $P > 0.05$).

The results show that the depression of the pyrogenal fever observed in rabbits after thyroidectomy is accompanied by a decrease in the frequency with which endogenous pyrogen can be detected in the blood of these animals. This suggests that depression of the formation of endogenous pyrogen plays an important role in the reduction of the rise of body temperature taking place in thyroidectomized rabbits after injection of bacterial lipopolysaccharide. The results described indicate the absence of tolerance during repeated injection of pyrogenal into thyroidectomized animals in conditions in which it was present in normal animals. This problem requires further study.

SUMMARY

As demonstrated in experiments on rabbits, a decrease of its pyrexial reaction following intravenous administration of bacterial lipopolysaccharide (pyrogenal) was accompanied in thyroidectomized rabbits by reduction of the frequency of detection of endogenous pyrogen in the blood.

Following daily administration of pyrogenal (for 7 days) in normal rabbits habituation (not immunological tolerance) to the preparation was revealed; no such state developed in thyroidectomized animals.

The reaction to the administration of the same serum, containing endogenous pyrogen, was the same in intact and thyroidectomized animals.

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