

CHANGES IN THE BLOOD AND TISSUE HISTAMINE CONTENT IN RABBITS WHEN SENSITIZED WITH STREPTOCOCCI COMBINED WITH HEART MUSCLE EXTRACT

G. S. Kozlov

UDC 616-002.77-092.9-07:616

The histamine concentration in the blood and tissues (myocardium, liver, kidney, spleen, lung) was investigated by a fluorometric method in rabbits receiving injections of streptococci combined with heart muscle extract repeated at intervals in order to reproduce experimental rheumatic fever. A significant increase in the histamine concentration in the blood and the kidney and liver tissues was found in the experimental animals. The histamine concentration in the spleen, however, was significantly lowered. Besides changes in the histamine concentration in the blood and tissues, the free histamine level in the serum also was changed in experimental rheumatic fever.

Systematic clinical investigations have demonstrated marked changes in histamine metabolism in patients with rheumatic fever [2].

Having regard to the etiological role of streptococci in rheumatic fever, the role of histamine in allergic inflammation, and its effect on vascular permeability [1, 6], in the investigation described below the histamine concentration was studied in the blood and organs (myocardium, liver, kidneys, spleen, lung) of rabbits receiving injections of group A β -hemolytic streptococci in conjunction with heart muscle extract in order to reproduce experimental rheumatic fever.

EXPERIMENTAL METHOD

Altogether, 33 experimental and 45 control rabbits (4 series of experiments) were investigated. Group A β -hemolytic streptococci (strains Nos. 2432 and 6339, "Ward," obtained from the L. A. Tarasevich State Control Institute of Medical Biological Preparations) were injected into the peritonsillar region and intraperitoneally in conjunction with extract of homologous heart muscle. Three cycles of injections were given. Each cycle consisted of six intraperitoneal injections of a 24-h culture of streptococci containing 3 billion bacterial cells once every 4-6 days, one injection of streptococci into the peritonsillar region, and two injections of 15% heart muscle extract intraperitoneally. The experiments lasted 6 months. Control rabbits were kept under identical conditions side by side with the experimental rabbits. During the experiment, a worsening of the animals' general condition was accompanied by changes in the blood biochemistry, almost one-third of the animals developed lesions of the joints, and at the end of the experiment endomyocarditis was detected histologically. Blood from the auricular vein was taken for analysis, and the organs to be studied were removed immediately after sacrifice, kept in the cold, and weighed samples were ground in a mortar with sand. Histamine was determined by a fluorometric method [7] in the blood of all animals, in the spleen of 21, in the lungs of 15, and in the myocardium of the left ventricle, the liver, and the kidneys of 18 rabbits from each group. The serum histidine concentration was investigated by paper chromatography [4].

Yaroslavl' Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 74, No. 9, pp. 35-37, September, 1972. Original article submitted November 2, 1971.

© 1973 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. All rights reserved. This article cannot be reproduced for any purpose whatsoever without permission of the publisher. A copy of this article is available from the publisher for \$15.00.

EXPERIMENTAL RESULTS

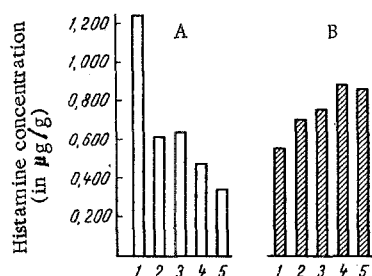


Fig. 1. Histamine concentration in tissues of control (A) and experimental (B) rabbits: 1) spleen; 2) lung; 3) heart; 4) liver; 5) kidney.

The histamine concentration in the blood and tissues of the experimental and control animals showed considerable fluctuations, in agreement with observations by other workers [3, 5]. The histamine concentration in the blood of the control rabbits was $0.647 \pm 0.046 \mu\text{g/g}$ body weight. In the experimental rabbits in which rheumatic fever was reproduced the histamine concentration in the whole blood was significantly increased to $1.108 \pm 0.097 \mu\text{g/g}$ ($P < 0.01$). The ratio between the histamine concentrations in the internal organs also was changed. By comparison with the intact animals, the histamine concentration showed a statistically significant increase in the liver and kidneys ($P < 0.05$ and $P < 0.01$ respectively). In the spleen, however, the histamine concentration per gram tissue was much lower in the experimental animals than in the controls ($P < 0.02$; Fig. 1).

The increase in the histamine concentrations in the blood and organs was probably due to the harmful action of streptococcal and tissue antigens and toxins on the tissue cells, leading to an increase in the liberation of histamine and its discharge into the blood stream. Accumulation of histamine in the kidneys could also be influenced by the raised blood histamine concentration, for under these circumstances the load on the kidney to excrete histamine is increased. So far as the spleen is concerned, the decrease in the histamine content per gram of spleen tissue was probably due to an immunological response to the repeated injections of streptococci and tissue antigen, accompanied by structural changes in the cells demonstrable morphologically. The spleen in the experimental animals was enlarged, an increase in the number of germinal centers in the follicles was observed histologically, and the follicles themselves were reduced in size. The ratio between the weight of the spleen and the total weight of the animal was $0.50 \pm 0.06 \text{ g/kg}$ in the control rabbits and $0.81 \pm 0.10 \text{ g/kg}$ in the experimental rabbits ($P < 0.05$).

Since histidine is the source of histamine, the histidine concentration in the blood serum was studied. The free histidine level in the blood serum was higher in rabbits with experimental rheumatic fever ($1.44 \pm 0.156 \text{ mg\%}$ in the intact animals and $2.076 \pm 0.171 \text{ mg\%}$ in the experimental rabbits; $P < 0.02$). Evidently a deficient utilization or deficient deamination and decarboxylation of histidine was present. There are therefore grounds for considering that the increase in the histamine concentration in the blood of rabbits with experimental rheumatic fever takes place mainly on account of increased liberation of histamine from the cells and not of its increased formation from histidine.

During repeated cycles of injections of streptococci together with heart muscle extract considerable changes thus take place in the histamine concentration in the blood and tissues. The disturbances are greater in the histamine metabolism in the spleen, an organ composed of lymphoid tissue and taking part in immunological reactions.

LITERATURE CITED

1. A. D. Ado, General Allergology [in Russian], Moscow (1970).
2. G. S. Kozlov and N. I. Korshunov, in: Proceedings of the 1st All-Union Congress of Rheumatologists [in Russian], Moscow (1971), p. 201.
3. M. D. Kyrstya, Uspekhi Sovr. Biol., 51, No. 1, 21 (1971).
4. T. S. Pashina, Quantitative Determination of Amino Acids by Paper Chromatography by the Method of Formation of Copper Derivatives of Amino Acids with Ninhydrin [in Russian], Moscow (1959).
5. V. I. Uspenskii, Histamine [in Russian], Moscow (1962).
6. N. G. Beall, Calif. Med., 106, 296 (1967).
7. P. A. Shore, A. Burkhalter, and V. H. Cohn, J. Pharmacol. Exp. Ther., 127, 182 (1959).