LOMA LINDA UNIVERSITY

Medical Arts and Sciences: A Scientific Journal of the College of Medical Evangelists

Volume 1 | Number 1 Article 5

4-1947

The Circulatory Effects of Histamine

Fred B. Moor
College of Medical Evangelists

CURRENT COMMENT

THE CIRCULATORY EFFECTS OF HISTAMINE*

FRED B. MOOR, M.D.

Few substances in the realm of biological chemistry have created more general interest than beta-iminazolylethylamine, commonly called histamine. It occurs in extracts of all animal and plant tissues, in which some is free and some results from protein cleavage. Its pharmacodynamics has been well elucidated, but its physiological significance is still largely theoretical. We are interested at this writing in the circulatory relationships of this interesting substance.

When applied locally by intracutaneous injection, by iontophoresis, or even by inunction, histamine produces a marked arteriolar and capillary dilatation with increased permeability of capillary walls and wheal formation. The wheal subsides in about half an hour, but redness and increase in skin temperature persist for a much longer period of time. It is also of interest to note that histamine applied by iontophoresis fails to produce marked local vasodilatation or wheal formation in areas where there is advanced occlusive vascular disease; in fact, this finding may be used as a measure of the circulatory impairment.

When a sufficient quantity of histamine gains access to the general circulation, as it may by subcutaneous, intramuscular, or intravenous injection, or by iontophoresis, systemic signs and symptoms arise, consisting of flushing of the face, a rise in skin temperature, a sharp drop in blood pressure, and a throbbing headache. Syncope occasionally occurs. With larger doses these signs and symptoms are all exaggerated, with the addition of bronchial constriction and dyspnea, vomiting and diarrhea. These manifestations are usually of short duration because of the rapid destruction of histamine, the compensatory increase in heart rate, and the sudden discharge of epinephrine, which is the specific physiological antagonist. In fact, this compensatory mechanism is so effective that a dilute solution of histamine given intravenously produces no marked change in the blood pressure.

On the physiological side Anrep *et al.* have demonstrated that histamine or a histamine-like substance is produced in muscle during exercise. These investigators considered histamine, by its vasodilating action, to be important in the physiological adjustment of the blood flow to the increased metabolic needs resulting from increased muscular activity. They also observed that a ten- to twenty-minute occlusion of the arterial blood supply to a limb caused a marked increase in the venous histamine level during the resulting reactive hyperemia. It appears, therefore, that histamine may have a definite physiological function to perform in augmenting the blood flow to meet local tissue requirements.

The recent report of Wirtschafter and Widmann on the treatment of the peripheral vascular diseases by the *in vivo* elaboration of histamine has added still further to the already widespread interest in this substance. After trying diethylether, with varying success, as recommended by Katz in the treat-

* From the Department of Therapeutics in the College of Medical Evangelists.

ment of these diseases, they reasoned that since Dale and Laidlaw had demonstrated that ether sensitized the capillaries to histamine, and since serum from some of their ether-treated patients produced cutaneous wheals and flares in nonallergic subjects and caused contraction of isolated guinea pig intestine, the favorable results in some patients might be due to the vasodilating action of histamine. From the work of Holtz they learned that the addition of ascorbic acid to histidine *in vitro* resulted in the production of histamine. By the simultaneous parenteral administration of large doses of histidine monohydrochloride and sodium ascorbate, Wirtschafter and Widmann were able to produce clinical improvement in eleven patients suffering from peripheral vascular disease, including seven with arteriosclerosis obliterans, two with thrombo-angiitis obliterans, and two with sudden arterial occlusion. They observed improvement of the peripheral circulation with relief of pain, increased warmth, and limitation of gangrene. Serum from these patients produced more marked cutaneous wheals and flares in nonallergic subjects than the serum from the ether-treated patients.

Although the ascorbic-histidine treatment of the peripheral vascular diseases is exceedingly interesting and appears physiologically sound, the present cost is prohibitive for many patients. If an adequate blood level of histamine is the only requisite for the successful treatment of these diseases, it seems that a simpler, easier, and cheaper method would be the administration of histamine itself by intravenous injection or by iontophoresis. By either of these latter routes any desired blood level could be maintained, although probably not as continuously as by the ascorbic-histidine procedure. Wirtschafter and Widmann have obviously made an important contribution to the therapy of the occlusive vascular diseases, which, as they have indicated, may be of value in the treatment of a number of other conditions in which the circulatory effects of histamine might be beneficial.

BIBLIOGRAPHY

Anrep, G. V.; Barsoum, G. S.; Solama, S.; and Souidan, Z.: Histamine liberation during reactive hyperemia and muscle contraction in man, J. Physiol. 103:297-305 (Dec.) 1944.

Dale, H. H., and Laidlaw, P.: Histamine shock, J. Physiol. 52:355-390 ( ) 1919.

Holtz, P.: Histaminbildung aus Histidin durch Ascorbinsaure, Naturwissenschaften 25:14 (Jan.) 1937.

Katz, R. A.: Impending ischemic gangrene; new nonsurgical therapeutic suggestions, New Orleans S. J. 98:542-555 (June) 1946.

Wirtschafter, Z. T., and Widmann, R.: The elaboration of histamine *in vivo* in the treatment of peripheral vascular disorders, J. A. M. A. 133:604-605 (March 1) 1947.