DETERMINATION OF SMALL AMOUNTS OF HISTAMINE IN BIOLOGICAL FLUIDS FROM ALLERGIC SKIN REACTIONS

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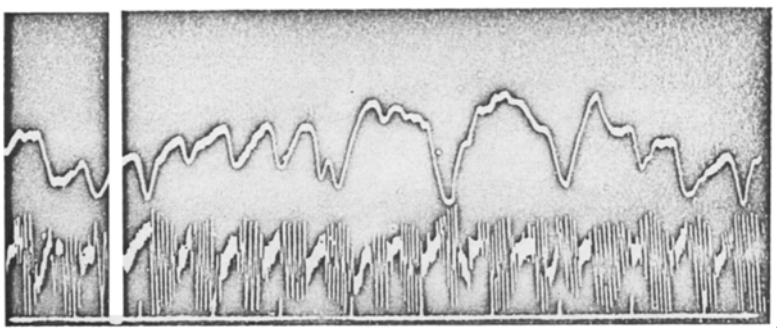
A prominent place is afforded to the elucidation of the role of histamine and of substances with a histamine-like action in the experimental and clinical study of the pathogenesis of allergic reactions. The authors of this paper have been required to determine very small amounts of such substances. The methods generally used do not, however, permit of the detection of such small amounts. Thus one of the most sensitive methods, depending on the reaction of isolated guinea pig intestine, permits of the detection of not less than 0.005 mg of histamine in a given solution (L. A. Olvin and V. I. Olvin). We have found that such doses of histamine do not cause any change in the blood pressure of cats.



Change in the rate of flow of blood through renal vessels of a dog after introduction of skin dialyzate from a nettle-rash patient.

In searching for a method enabling us to detect very small amounts of histamine, we directed our attention to the very high sensitivity to histamine of the renal blood vessels. These are dilated by histamine in dilutions of $1:10^{-6}$ to $1:10^{-7}$ which have no perceptible effect on systemic pressure. This leads to an increased rate of flow through the renal blood vessels. We measured the rate of flow by means of a Rein diathermic flow-meter. A special electrode is placed on an exposed, but not opened, artery, and the blood flowing through it is heated by means of a high frequency current. This gives rise to a temperature difference between the blood distal and proximal to the electrode. The faster the blood flow, the less time it spends in the high frequency field, and the smaller is the temperature difference. This temperature difference is picked up by a thermocouple mounted into the electrode, and the readings are recorded through a galvanometer on a moving photokymograph strip. Simultaneously with the measurement of blood flow, we registered blood pressure, under Hexenal anesthesia.

by means of an optical manometer. The electrode of the Rein flow-meter was inserted through an abdominal incision, and placed on the renal artery. The test solution was introduced into the iliac vein. The presence of histamine or of a histamine-like substance was indicated by increase in the rate of flow through the renal artery.

We tested skin dialyzates from normal controls (9 tests) and from patients suffering from nettle-rash, taken from unaffected parts of the skin (4 specimens) and from the urticarial wheals (10 specimens). The skin dialyzates were prepared in the following way. A glass cup, with a base diameter of 38 mm, covering a skin area of 10.33 cm^2, was fastened to the selected surface with an elastic tape. The cup was filled through an opening at its top with 6 ml physiological saline, which remained in contact with the skin for 30 minutes, after which it was pipetted out. The dialyzate thus obtained was taken for injection with no further treatment. The amount injected for test was 1-3 ml. Apart from this, we made a number of tests of edema fluid, aspirated from the wheals by means of a fine needle. For purposes of comparison, we determined the action of 1 ml of histamine solutions, in dilutions of 1 : 10,000 and 1 : 10,000,000. In all, we performed 28 tests.

Our tests showed that the dialyzates from freshly erupted urticarial wheals contain substances which increase the rate of flow of blood in the renal artery, without affecting the systemic blood pressure. This effect was absent from material from healthy controls and from the unaffected parts of the skin of nettle-rash patients. Tests conducted with standard solutions of histamine showed that an effect of the same order as that given by the urticarial dialyzates was given by dilutions of $1 : 10^{-7}$.

Substances exerting a histamine-like action on the artery were detected in the edema fluid aspirated from the wheals. This finding confirms the view that urticarial wheals are the result of an angioneurosis, due to the histamine-like action of the edema fluid.

SUMMARY

A method of determination of histaminic activity in biological fluids (corresponding to contents of histamine equal to $1 : 10^{-7}$) is described. This method consists of determination of the changes of velocity of the renal blood flow under the effect of histamine in dogs. The vascular reaction is registered by the change of blood flow velocity with the aid of Rein's flow-meter. The data obtained verify the presence of histaminic activity in the fluid derived from urticarial vesicles.

LITERATURE CITED

[1] I. A. Olvin and V. I. Olvin, Vestnik. Venerol. i Dermatol., No. 6, pp. 12-15 (1949).