

## ACTION OF HISTAMINE ON THE CAROTID SINUS OF THE DOG

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Histamine plays a definite part in the development of various kinds of shock. When injected parenterally, it produces a condition which in many respects resembles anaphylactic shock.

An important feature of its action is its influence on effectors but scarcely any attention has been paid to its possible influence on reflex effects from the interoceptors; nevertheless, Lewis [8], as far back as 1927, showed the importance of the axon reflex in the action of histamine on capillaries. According to Landgren and others [7], 2-50  $\gamma$  of histamine produces no stimulant effect on the chemoceptors of the carotid sinus. However, the same amount of histamine is effective in stimulating the receptors of the intestine and spleen [3]. A greater amount (5 mg) causes marked reflex changes in respiration and arterial pressure through acting on the interoceptors of the limb vessels [10].

Published reports [2, 4, 5] have shown that substances which affect the contraction of the smooth muscle of blood vessels, also exert an influence on the mechanoreceptors of the carotid sinus and aorta.

These receptors are intimately concerned in the maintenance of the arterial pressure [3], and because histamine can influence the contraction of the smooth muscle of many organs, we decided to examine its action on the depressor receptors of the carotid sinus.

### METHOD

The influence of histamine on arterial pressure was studied in 15 dogs, 6 of which were sensitized to horse serum 16-23 days previously; they received 0.2 ml of serum per kg subcutaneously on two successive days.

Morphine-pentothal anesthesia was used. The carotid sinus was exposed, and the arterial pressure measured with a mercury manometer either from the common carotid artery of the same side, or from the femoral artery.

The sinocarotid pressor reflex was induced by lowering the pressure in the carotid sinus by compressing the common carotid. The depressor sinocarotid reflex was produced by a stepwise increase of 20 mm at a time of the pressure of the pressure in the sinus, using a modification of the method of Lim and Chang [9]. The method allowed the increase in volume of the carotid sinus in response to pressure changes to be determined (Fig. 1). The method was accurate to  $\pm 0.0025$  ml.

To determine the action on the smooth muscle of the carotid sinus of whole horse serum and of 0.25 ml of 0.1% solutions of histamine and adrenalin, the wall of the carotid sinus and adjacent parts of the carotid artery were infiltrated with these substances.

### RESULTS

There was no difference in the reflex response to histamine between the normal and the sensitized animals, and the results for the two groups have been placed together.

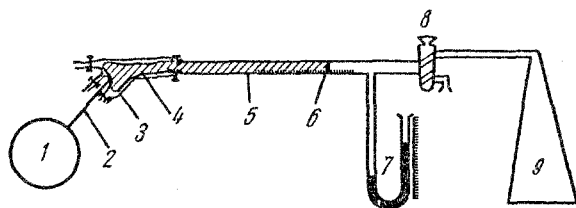


Fig. 1. Diagram of the apparatus for recording the effect of pressure changes on carotid sinus volume. 1) Vasomotor center; 2) nerve supplying sinus; 3) carotid sinus; 4) rubber balloon introduced into carotid sinus; 5) cannula with scale divisions, filled with physiological saline and connected to the balloon within the carotid sinus; 6) meniscus of physiological saline, movement of which indicates variation in sinus volume; 7) manometer; 8) two-way tap connecting cannula either with atmospheric pressure or with compressed air supply; 9) cylinder with compressed air.

40% of the experiments, after histamine action it was found that there was a slower increase in volume over the pressure range of 80 to 120 mm, but with higher pressures, the volume of the histamine-treated preparations increased more rapidly (Fig. 2, A). This can be very well seen on the trace for the "volume elasticity" given by Landgren [6] and (Fig. 2, B).

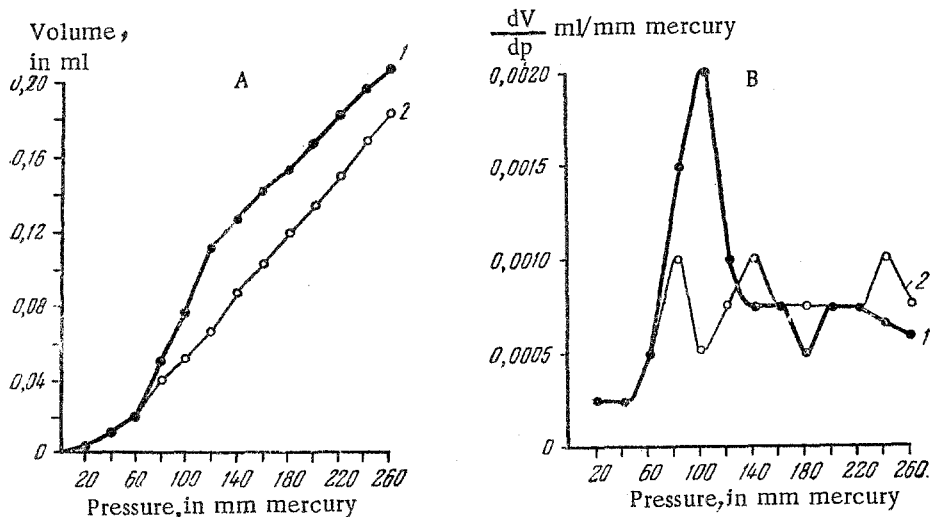


Fig. 2. Effect of histamine on the elasticity of the carotid sinus wall. A) Increase in carotid sinus volume due to increased internal pressure; B) change in the "volume elasticity". 1) Before, 2) after the action of histamine.

Although in histamine hypotension the pressor response to a lowered carotid sinus pressure is reduced, we never found it to be entirely absent, as did A. D. Ado and M. A. Erzin [1] after the anaphylactic reaction, and Heymans [5] after the action of adrenalin on the carotid sinus.

In comparing the reflex hypotensive effects of histamine and adrenalin, it is immediately apparent that adrenalin is the more active substance. It produces a greater change which lasts for a longer time. When histamine is added to a carotid sinus already infiltrated with adrenalin, no blood pressure change occurs.

In most cases, the effect of histamine on the carotid sinus was to reduce the arterial pressure. In experiments where circulation through the sinus was maintained, there was the possibility of absorption of histamine into the blood stream. However, even when no blood passed through the sinus, infiltrating the wall with histamine also produced a reflex hypotension, (Fig. 3, a).

Section of the sinocarotid nerve or infiltrating the wall of the sinus with novocain solution eliminates the reflex hypotension. The amount by which the pressure fell varied from 4 to 30 mm, representing 3 to 18% of the original arterial pressure. The change lasted from 7 to 20 minutes or more. In one case, there was an increase in arterial pressure of 9 mm which lasted for 1.5 minutes. There were other cases in which no change occurred.

A study of variation of the elasticity of the carotid sinus wall showed that in 60% of the cases histamine produced no change. In the remaining

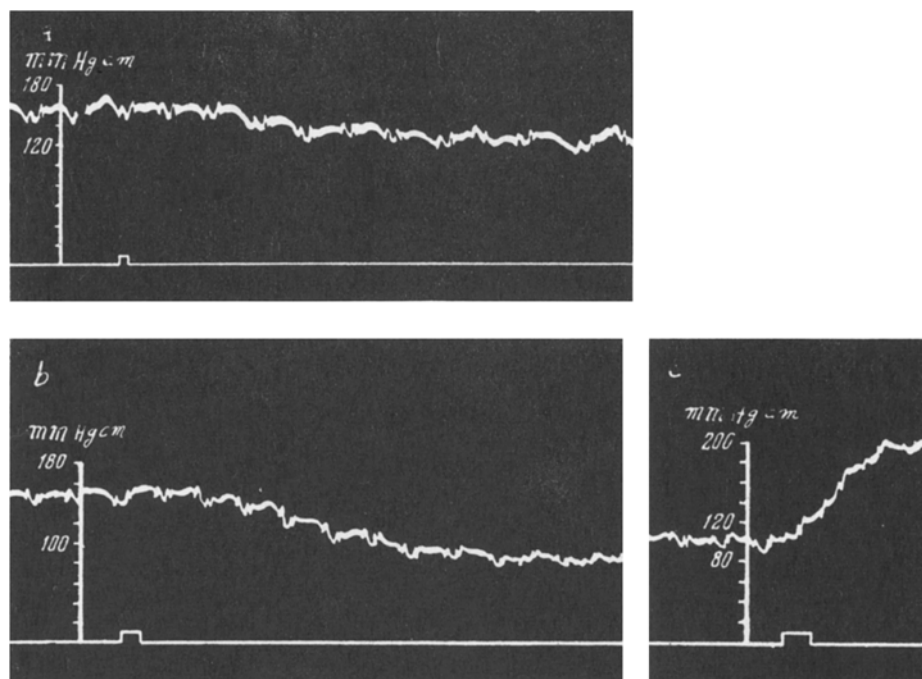


Fig. 3. Arterial pressure change on infiltrating the wall of the isolated carotid sinus with histamine and with adrenalin. Dog, weight 15 kg. Vagi sectioned in neck. Tracing on millimeter paper, speed 1 mm/second. a) Infiltrating the wall of the isolated carotid sinus with 0.25 ml of 1:1000 histamine. Reduction of arterial pressure by 30 mm mercury. b) 30 minutes later. Arterial pressure has returned to the initial value. Infiltration of the carotid sinus wall with 0.25 ml of 1:1000 adrenalin causes a reduction in arterial pressure of 60 mm mercury. c) 40 minutes after the action of adrenalin. The arterial pressure has not returned to the initial value. Infiltrating the wall of the carotid sinus with 2.5 ml of 0.5% novocain inhibits the reflex hypotension.

On the other hand, a definite hypotensive reflex occurs if adrenalin is added to a carotid sinus already treated with histamine. Similarly, histamine is without effect in sensitized dogs in whom reflex hypotension has been induced by treating the carotid sinus with horse serum.

Thus, histamine is a less effective stimulus for the depressor mechanoreceptors of the carotid sinus than is adrenalin or the permissible dose of serum. It seems probable that histamine does not play any important part in the development of the reflex "sinus shock" [1].

#### SUMMARY

In most instances infiltration of the carotid sinus wall with histamine causes a reflex drop of arterial pressure the intensity and duration of which is lower than in the case of hypotension produced by the adrenalin action on the smooth muscles of the carotid sinus.

No connection was revealed between the carotid sinus wall expansion and the depressor reflex.

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