Use of New Technic to Study Humoral Transmission of Hypertensive Effects of Vagal Stimulation. (21220)

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(Introduced by S. Ochoa.)

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We have previously shown(1-3) that stimulation of the central end of the cut cervical vagus nerve leads to the liberation of a hypertensive substance. The blood collected during the hypertensive phase has hypertensive effects under various experimental conditions. With 2 dogs linked in cross-circulation, vagus stimulation in one of them produces increased blood pressure in the other. This result is not modified by the insertion of a flow-regulating meter in the blood circuit between the 2 animals to avoid changes in pressure due to variations of flow. A number of observations suggested that the hypertensive substance, which resembles noradrenaline in pharmacological properties, is liberated from the arterial walls. Our results could not be explained by the assumption of Taylor *et al.*(4) that the hypertensive factor arises from the brain or the pituitary gland.

By use of a new cross-circulation technic we have confirmed our earlier results and obtained some further support for the arterial origin of the hypertensive substance.

Technic. The aortae of 2 dogs were sectioned and anastamosed with cannulae in such a way that the proximal end of the aorta of dog A was connected to the distal end of the aorta of dog B and conversely (Fig. 1). A flow regulator was inserted in the circuit and adjusted so that each dog lost as much blood as it received (90 to 110 ml/min.). The blood pressure was registered simultaneously in the femoral arteries or in both carotid and femoral arteries of each dog. The vagus was stimulated with an electronic stimulator as in previous experiments.

Results. Effect of stimulation of central end of vagus. Stimulation of the central end of the vagus of one of the dogs produces an increase in blood pressure in the carotid and femoral arteries of this dog followed by a smaller increase of pressure in the femoral artery of the second dog. There is no change in the carotid blood pressure of the latter animal. The pressure increase is greater in the carotid than in the femoral artery of the stimulated dog. These results are illustrated in Fig. 2 and 3.

Effect of noradrenaline. Injection of noradrenaline (100 μg) into the femoral vein of one of the dogs produces an increase of blood pressure in the carotid, but not in the femoral artery of this animal followed by an increase in the femoral arterial pressure of the second dog (Fig. 4). This result is easily understood as the injected noradrenaline passes through the central aorta to the femoral of the other dog before the blood reaches the injected dog's own femoral artery.

Discussion. The above results can best be interpreted by the assumption that stimulation of the central end of the vagus causes the liberation of a hypertensive substance (prob-

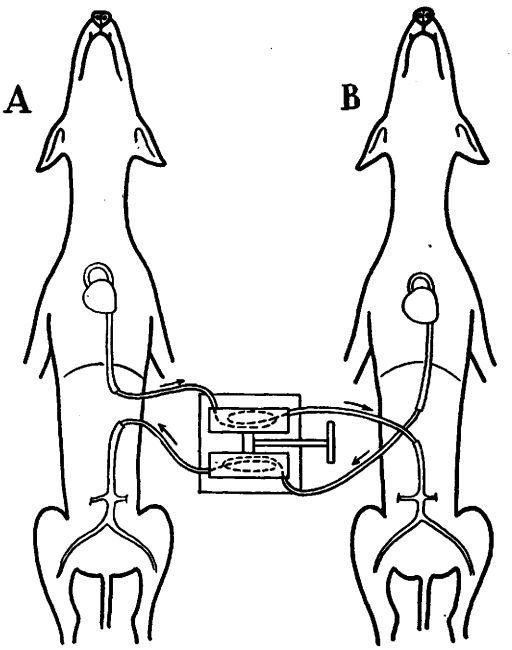

FIG. 1.
Diagram illustrating cross-circulation technic.

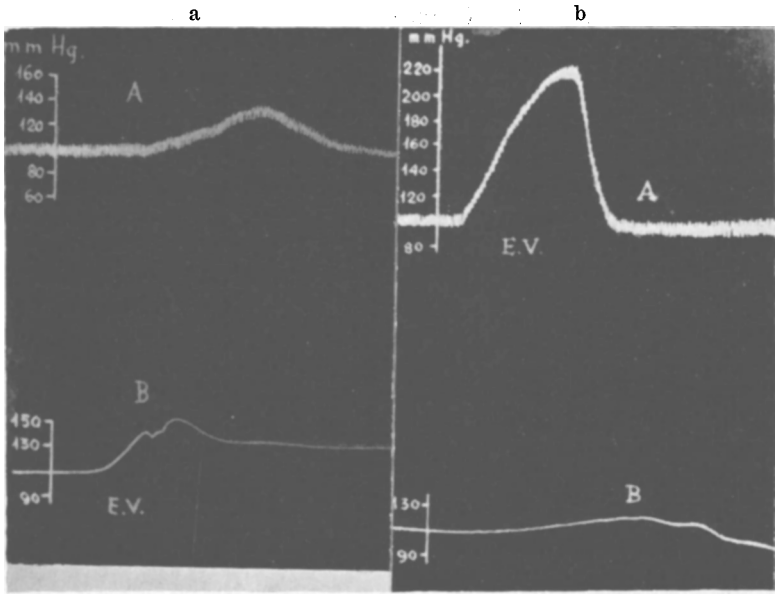

FIG. 2a. Blood pressure tracings showing effect of stimulation of central end of vagus of one dog. B. Femoral artery of stimulated dog. A. Femoral artery of the other animal. Fig. 2b. As 2a. A. Carotid artery of stimulated dog. B. Femoral artery of the other animal.

ably noradrenaline) from the arterial walls themselves. If stimulation led to the liberation of a substance of encephalic or hypophyseal origin (or derived from another organ) into the venous circulation one would expect the results of the stimulation to mimic those obtained after the intravenous injection of noradrenaline, *i.e.*, increase of pressure in the carotid, but not in the femoral artery of the treated dog, followed by increase in the femoral pressure of the untreated one. One would not expect an increase in both carotid and femoral arterial pressures of the stimulated dog as was actually observed.

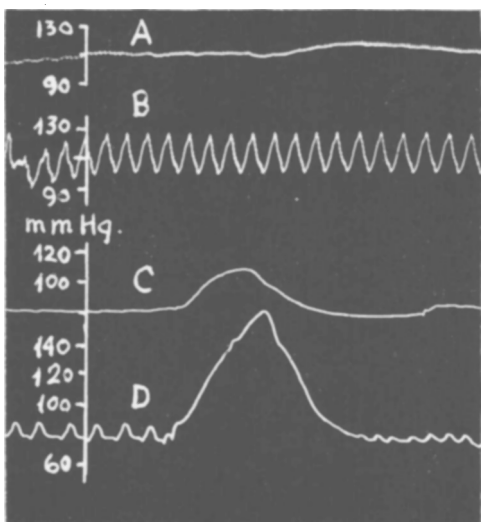

FIG. 3. As Fig. 2. C and D, femoral and carotid arteries respectively of stimulated dog. A and B, femoral and carotid respectively of the other animal.

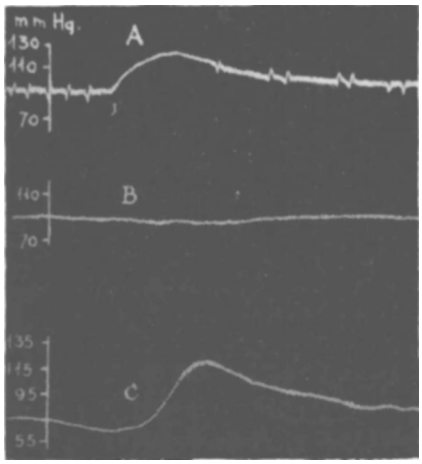

FIG. 4. Blood pressure tracings showing effect of intravenous injection of 100 μg of noradrenaline into one dog. A and B, carotid and femoral artery respectively of injected dog. C, femoral artery of the other animal.

Summary. Experiments on dogs linked in cross-circulation, by connecting the central end of the aorta of one dog to the peripheral end of the aorta of the other and vice versa, have confirmed earlier results in this laboratory indicating that a hypertensive substance is liberated on stimulation of the central end of the cut vagus nerve. Comparison of the results of the vagus stimulation and noradrenaline injection have provided further evidence for the assumption that the hypertensive substance is probably liberated from the arterial walls themselves.

1. Jiménez Diaz, C., de la Barreda, P., Souto, J., and Alcalá, R., *Bull. Inst. Med. Res. Univ. Madrid,* 1950, v3, 131.

2. Jiménez Diaz, C., de la Barreda, P., Molina, A. F., and Alcalá, R., *Ibid.,* 1951, v4, 167.

3. de la Barreda, P., Molina, A. F., Alcalá, R., and Jiménez Diaz, C., *Ibid.,* 1952, v5, 65.

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Effects of Ouabain on Beat and Oxygen Consumption of Embryonic Chick Hearts.* (21221)

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Friedman and Bine(1) demonstrated that the embryonic duck heart is very sensitive to digitalis preparations. Preliminary experiments showed us that embryonic chick hearts, although not as sensitive to digitalis as embryonic duck hearts, are, nevertheless, satisfactory in this respect, easier to obtain, and less expensive. The cartesian diver technic is admirable for measuring metabolism of minute tissues. Further preliminary experiments showed that it could be adapted to measuring oxygen consumption of relatively large embryonic chick hearts weighing as much as 400 μg, dry weight, after 6 days of incubation. In another communication(2) we describe the necessary basic modifications for measuring oxygen consumption of embryonic chick heart with the cartesian diver.

Methods. The cartesian diver with a shaker and divers with caps and mixers(2) was employed. Fertile chicken eggs were incubated 5 days, producing embryos with hearts of maximum size (80 to 300 μg, dry weight), which would beat regularly and reliably. These hearts were dissected into Ringer or other suitable solution until needed. The solutions were kept at 37°C. A heart was placed in the bulb of a diver, 10 mm^3 of Ringer or other suitable solution was added. Air was replaced by 100% oxygen. Exactly one mm^3 of same solution (control) or of a solution containing ouabain was deposited on surface of the neck, and a magnetic mixer placed in this droplet. After reoxygenating, adding the KOH seal, and placing a buoyed cap on the diver, it was immersed in the flotation medium in a diver holder. About 10 minutes was allowed for temperature equilibration at 37.3°C. Observations on rate and regularity of the beat were made on the odd numbered minutes, and measurements of suspension pressures made on even numbered minutes for 42 minutes, then at less frequent and less regular intervals up to 4 hours. Mixing was performed at 11 minutes as described elsewhere(2). Changes in suspension pressures were corrected for changes in barometric pressure and were multiplied by the diver constant to give oxygen consumption. At the close of each experiment the hearts were weighed on a quartz fiber balance; all oxygen consumption figures were converted to mm^3/mg of dry weight. The results of comparable experiments were averaged.

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