

THE REFLEX EFFECT OF CERTAIN DRUGS  
ACTING ON THE RECEPTORS OF THE  
MESENTERIC VEINS IN THE CAT

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(Received February 16, 1959. Presented by Active  
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The presence of receptors in the veins, reacting to various chemical stimuli, has been demonstrated by a number of investigations [1, 2, 5, 7, 8, 9, 10, 11]. In our previous research [3, 4] we showed that adrenalin, strophanthin, and certain other drugs, acting on the receptors of the lateral thoracic vein of the rabbit and the subcutaneous femoral vein of the cat, bring about a slowing of the heart rate, a fall in the arterial pressure, and depression of respiration, but when acting on the receptors of the femoral vein in the frog they depress respiration and elicit a generalized motor reaction but do not change the rate of the heart.

The present work is a continuation of the above-mentioned research.

EXPERIMENTAL METHOD

Experiments were carried out on cats in order to study the reflex effects of drugs acting on the receptors of the mesenteric vein, using the method of perfusion of a humorally isolated segment of vein. The humoral isolation of an area of the mesenteric vein was carried out under urethane anesthesia by the method suggested by B. Z. Sirotin [6]. After the animal had been fixed to the bench, a 10% solution of urethane was injected intraperitoneally in a dose of 1-2 g/kg body weight. The animal was subsequently maintained in a state of light anesthesia by injections of small doses of the anesthetic.

Ringer's solution or the test solutions were passed through the humorally isolated segment of the mesenteric vein, 8-12 cm in length. The level of the solutions was maintained 10-12 cm above the perfused segment of vein and was unchanged throughout the experiment.

As a result of the free drainage, the pressure in the isolated segment of vein did not exceed the blood pressure in the other veins of the peritoneal cavity of the animal, as was shown by the entry of blood into the perfusion fluid from small divided vessels. The aerated solutions (test and Ringer's) were warmed to 37-38° before being introduced into the segment of the vein. After the perfusion had begun, the intestine was replaced in the peritoneal cavity, where it remained throughout the experiment.

Changes in the activity of the heart were recorded by an EKP-4 electrocardiograph. The action potentials of the heart were picked up by means of needle electrodes introduced beneath the skin corresponding to lead 2. The electrocardiogram was recorded several times before application of the stimulus, during stimulation, and after the chemicals had been rinsed out with Ringer's solution. Continuous kymographic tracings of the arterial pressure in the carotid artery were made with a mercury manometer and of the respiration through a tracheal cannula.

In each experiment from 2 to 7 tests were made of the reflex effect of the test substances (the same or different). When different substances were tested, the order of their application in the experiments was changed.

TABLE

Reflex Changes in the Heart Rate, Arterial Pressure, and Respiration in Response to Stimulation of the Receptors of the Mesenteric Vein of the Cat

Drug tested	Heart rate			Arterial pressure			Respiration		
	slowing	no change	quicken.	decrease	no change	increase	de- pression	no change	excitation
Adrenalin	6	2	4	—	10	8	—	11	9
Strophanthin	10	3	8	8	10	2	7	15	2
Caffeine	12	3	4	12	12	1	7	12	2
Glyceryl	4	1	5	6	10	—	5	10	—
Cardiazol	4	1	2	7	6	1	8	3	2
Total number of tests	70			93			93		

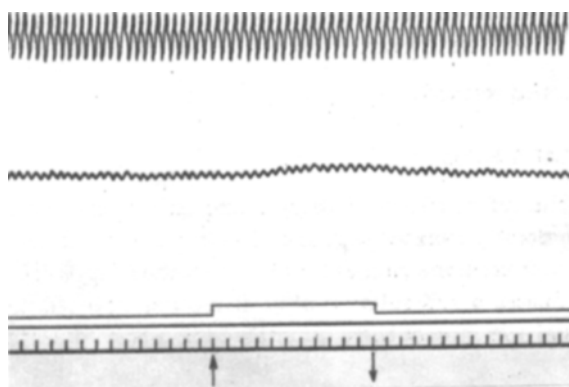


Fig. 1. The reflex effect of a  $1:10^6$  adrenalin solution from the receptors of the mesenteric vein of a cat on the respiration and arterial pressure. Significance of the curves (from above down): respiration, arterial pressure, stimulus marker, zero line, time marker (10 seconds). The arrows indicate the time of perfusion of the drug and of rinsing it out.

ments and did not exceed 10-15 beats per minute. In only one experiment did caffeine increase the heart rate by 25 beats. A second test of caffeine in the same experiment, instead of increasing the heart rate, decreased it by 7 beats. We observed this inconstancy of reflex action on the heart rate in many experiments in which the effect of other drugs besides caffeine was tested.

Thus in experiments on the mesenteric vein of the cat, as in those on the lateral thoracic vein of the rabbit and the subcutaneous femoral vein of the cat [3], results were obtained which show the absence of any specific, strictly purposeful reflex effect from the receptors of the veins on the activity of the heart.

As stimuli of the receptors of the mesenteric vein we used drugs having a marked action on the cardiovascular and respiratory systems when administered to the animal. The reflex effect of the following drugs was studied: adrenalin hydrochloride in a dilution of  $1:10^6$ , caffeine sodium benzoate —  $1:10^3$ , strophanthin —  $1:2 \cdot 10^6$ , glyceryl trinitrate —  $1:2 \cdot 10^5$  and cardiazol —  $1:2 \cdot 10^6$ .

#### EXPERIMENTAL RESULTS

The method of perfusion of the humorally isolated mesenteric vein was used in investigations on 20 cats. The results of the experiments are shown in the table.

Adrenalin, strophanthin, glyceryl trinitrate, and cardiazol, in roughly the same number of tests, caused either a reduction in the heart rate or an increase. A more definite result was given by caffeine which slowed the heart rate in 12 tests, quickened it in 4, and left it unchanged in 3 tests. The reflex changes in the activity of the heart by the action of the test drugs on the receptors of the mesenteric vein were insignificant in our experi-

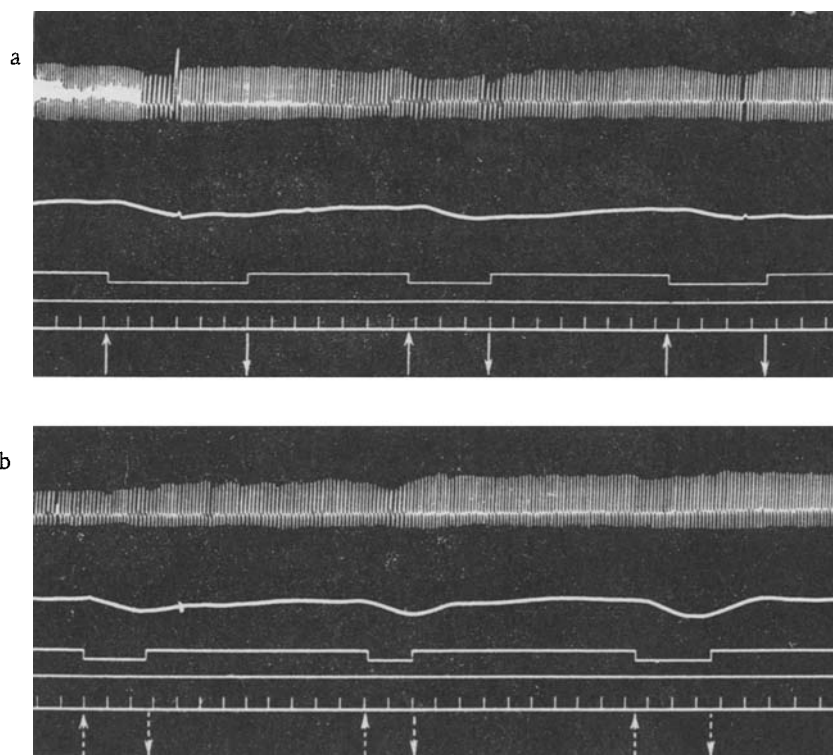


Fig. 2. Reflex effect from the receptors of the mesenteric vein on the respiration and arterial pressure of a cat.  
a) Injection of  $1:2 \cdot 10^6$  cardiazol solution; b) injection of  $1:10^3$  caffeine solution. Significance of the curves as in Fig. 1.

Qualitative changes in the electrocardiogram were studied from the results of 18 experiments. We could not detect any characteristic changes connected with the action of any of these drugs on the receptors of the mesenteric vein. During quickening and slowing of the heart rate the P wave was diminished, but the R and T waves and the S - T interval showed inconstant changes.

The direction of the reflex changes in the arterial pressure and respiration are shown in the table. The most obvious effect from the receptors of the mesenteric vein on the arterial pressure and respiration was shown by adrenalin. In almost one half of the tests it caused an increase in the arterial pressure by 5-10 mm Hg and strengthening of respiration. Adrenalin did not lower the arterial pressure in any experiment, nor did it depress respiration. In the majority of effective tests of the action of strophanthin, caffeine, glyceryl trinitrate, and cardiazol on the receptors of the mesenteric vein the arterial pressure was lowered by 5-30 mm Hg and the respiration was depressed.

By the action of the test drugs on the receptors of the mesenteric vein, changes developed gradually in the arterial pressure, which then returned smoothly to its initial level (Figs. 1, 2). In some experiments, after the first wave of fall or rise of arterial pressure, coinciding in time with the action of the stimulus on the receptors, a second fall or rise of arterial pressure ensued while the vein was being rinsed with Ringer's solution.

In the majority of tests the fall in arterial pressure was accompanied by depression of respiration, or sometimes by excitation. In some experiments changes occurred in the arterial pressure while respiration remained unchanged (see Fig. 1). In other experiments obvious changes developed in the respiration although the arterial pressure remained constant. The changes in respiration and arterial pressure did not always coincide in duration.

After the repeated use of the same drug as a stimulus of the receptors of the mesenteric vein, a gradual diminution of the reflex response was observed, in some cases as far as absence of reaction to this stimulus. Perfusion of the isolated segment of vein with another drug, however, caused reflex reactions for a further few tests. Sometimes, in response to the repeated testing of the same drug, the first test gave no reaction, the second gave a reaction in one direction and the third, a reaction in the opposite direction.

Changes in respiration in response to the action of the drugs on the receptors of the mesenteric vein usually developed gradually and recovered smoothly. In most experiments simultaneous changes were observed in the depth and rate of respiration (see Fig. 2), but in some cases reactions affecting either the depth or the rate of respiration were seen.

The facts and experimental findings described show that perfusion of the humorally isolated segment of the mesenteric vein of the cat with the drugs that were studied may give rise to obvious changes in the arterial pressure and respiration. In order to prove their reflex nature, 5 control experiments were carried out in which the function of the receptors was blocked with 2% procaine, and 2 experiments in which labeled phosphorus  $P^{32}$  was used for this purpose. When the isolated segment of vein was perfused with the drugs after perfusion with 2% procaine solution for 10 minutes, no reflex changes were produced in the arterial pressure or respiration. In samples of blood taken from the subcutaneous femoral vein of the cat after perfusion of the isolated segment of mesenteric vein with the phosphorus isotope, the number of impulses per minute showed no increase after 15, 30, 60, and 120 minutes. The method which we adopted gave assurance of the humoral isolation of the isolated segment of vein, while preserving its nervous connections with the rest of the body intact, so that the reactions observed were reflex in nature.

The results of these experiments suggest that the reflexogenic zone of the intestinal veins plays a part in the mechanism of action of drugs entering these veins after absorption from the intestine.

#### SUMMARY

By employing the perfusion method of the humorally isolated portion of the anterior mesenteric vein in cat the author studied the reflex effect of solutions of adrenalin ( $1:10^6$ ), caffeine sodium benzoate ( $1:10^3$ ), strophanthin ( $1:2 \cdot 10^6$ ), glyceryl trinitrate ( $1:2 \cdot 10^5$ ) and cardiazol ( $1:2 \cdot 10^6$ ) on the heart rate, arterial pressure, and respiration. Adrenalin provoked a rise of arterial pressure and stimulation of respiration by reflex action, while other substances mostly reduced the arterial pressure and depressed the respiration. Caffeine frequently decreased the rate heart. The reflex origin of these reactions was proved by control experiments with 2% procaine solution and labeled phosphorus  $P^{32}$ .

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