# THE ACTION OF SOME CARDIAC DRUGS UPON THE CORONARIES OF A DOG

## ELECTROCARDIOGRAPHIC STUDIES UTILIZING ALSO A KINESCOPE

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At the base of numerous cardiovascular diseases lies a disturbance of the coronary circulation. For a study of the functional condition of the coronary vessels it is essential to have uninterrupted and continuous prolonged registration of changes. As previously reported [1], our laboratory employed kinescopic methods of observing cardiac vessels utilizing a pericardial cannula.

In the present study there was simultaneous observation of the width of blood vessels on heart surface and electric currents while influenced by the introduction of certain cardiac drugs.

## EXPERIMENTAL METHOD

Eleven dogs weighing 8 to 17 kg were utilized. Operations were performed under morphine-urethane narcosis. Observations on the blood vessels were made several hours after surgery. All dogs, 1-2 days before kinescope procedures, had ECG taken in leads I, II, III, and also from the chest. Before introducing any drug, the base condition of the blood vessels was recorded both kinescopically and by synchronous ECG in the chest lead.

The kinescope was introduced by a shortened pericardial cannula 34 mm in diameter made of plexiglass.

The cannula was placed over the left coronary vessel below its bifurcation into the circumflex and descending branches. To obtain measurements of pictures made, enlargements were obtained. To measure the left coronary, 100 frames were observed which corresponds to four seconds.

Observations were made before introduction of drugs and at varying intervals after their introduction (after 30 sec, 1, 3, 5, 8, 10, 20, 30, 40 minutes and longer). In some experiments a measurement was taken over 200 frames (i. e., an 8 second length of time).

The drugs – adrenalin, ephedrine, atropine, caffeine, and hypotonin [12] – were introduced into the femoral vein; Validol and nitroglycerin were placed on the sublingual mucous membrane.

Results are summarized in the table.

In Figure 1 are shown the curves of the changes portraying diameter alterations of the coronary arteries under the influence of various drugs in six experiments (A, B, C, D, E and F).

Changes in the Blood Vessels Under the Influence of Drugs

| Substance | Condition of vessels* | | No. observations | Dose introduced of substance | Length of observation in minutes |
|---|---|---|---|---|---|
| | widening | narrowing | | | |
| Adrenalin (0.1%) | 4 | 1 | 5 | 0.01 cc/kg to 0.3 cc/kg | 62 |
| Validol | 1 | 1 | 2 | 3-4 drops | 20 |
| Nitroglycerin (1%) | 1 | – | 1 | 3-4 drops | 24 |
| Hypotonin | 4 | 1 | 5 | 3 mg/kg to 6 mg/kg | 78 |
| Ephedrine (5%) | 2 | 1 | 3 | 0.1 cc/kg to 0.13 cc/kg | 34 |
| Caffeine (10%) | 2 | – | 2 | 0.1 cc/kg and 0.13 cc/kg | 55 |
| Atropine (0.1%) | 1 | 1 | 2 | 0.1 cc/kg | 46 |

*Figure indicates number of observations

The action of adrenalin is characterized by wide fluctuations in the width of the vessels during the course of the experiments, causing the "cog-wheel" type of curve.

In Experiments A and E (Figure 1) the maximum widening was observed in the first minute. In Experiments C and D the greatest change occurred in 10-15 minutes. Experiments B, C and D (Figure 1) were characterized by the alternating widening and narrowing of the arteries, the arterial width changing 2 and 3 times; in Experiment B the adrenalin action began while the artery was in the narrowing phase.

Several minutes after the introduction of adrenalin, while in the period of greatest arterial dilation (Experiment A), the PQ interval diminished from 0.1-0.09 ; QT interval diminished from 0.22 to 0.20; the QRS complex remained unchanged. The voltage of P rose from 2 to 4 mm; voltage of R rose from 8 to 12 mm; deflection T dropped from 9 to 4 mm.

In the period of the first arterial narrowing (after 25 min) the QRS complex increased (from 0.05 to 0.07); voltage of R dropped from 9 to 5 mm.

Ephedrine (Figure 1) caused widening in two experiments and in one (Experiment C) narrowing to the vessels. At the time of greatest vessel dilatation (Experiment F) QT interval diminished from 0.27 to 0.22.

Under the influence of nitroglycerin (Figure 1) by the 11th minute at time of maximum widening of the artery, P rose from 0.5 to 3 mm, and R from 7 to 11 mm.

Validol (Figure 1) in one experiment caused a gradual dilation reaching a maximum at 20 minutes. In another experiment (Experiment A) introduction of Validol produced a biphasic action – narrowing, followed by dilation. In the period of greatest narrowing of the arteries, R voltage fell to 4 mm. When the diameter of the arteries increased, R rose to 10 mm.

Caffeine (Figure 1, D and F) widens the coronary vessels. The maximum widening appeared by the 20th (Experiment D) and 30th minutes (Experiment F) from time of injection. The ECG records of diminution of the QRS complex and the QT interval, while R rose from 9 to 11 mm.

Atropine (Fig. 1,E) introduction is accompanied by arterial widening (Experiment F and also a narrowing (Experiment E). In both cases systole is lengthened. The voltage is substantially unchanged.

Hypotonin (Figure 1) in 4 out of 5 cases dilated the vessels. The maximum arterial widening occurred under the influence of hypotonin (1% solution in dose of 6 mg/kg) in Experiment D at the 16th minute following introduction of the solution. By the 30th minute there began a narrowing of the vessel (as compared with original state). In Experiment F after the contraction 56 minutes elapsed before widening began again. Figure 2,B and C show pictures taken of the blood vessels (Experiment D). Ten minutes after the introduction of hypotonin both the arteries and the veins dilated. The ECG showed increased voltage of R from 3 to 5 mm, P from 2 to 3 mm, T from 2 to 3 mm.

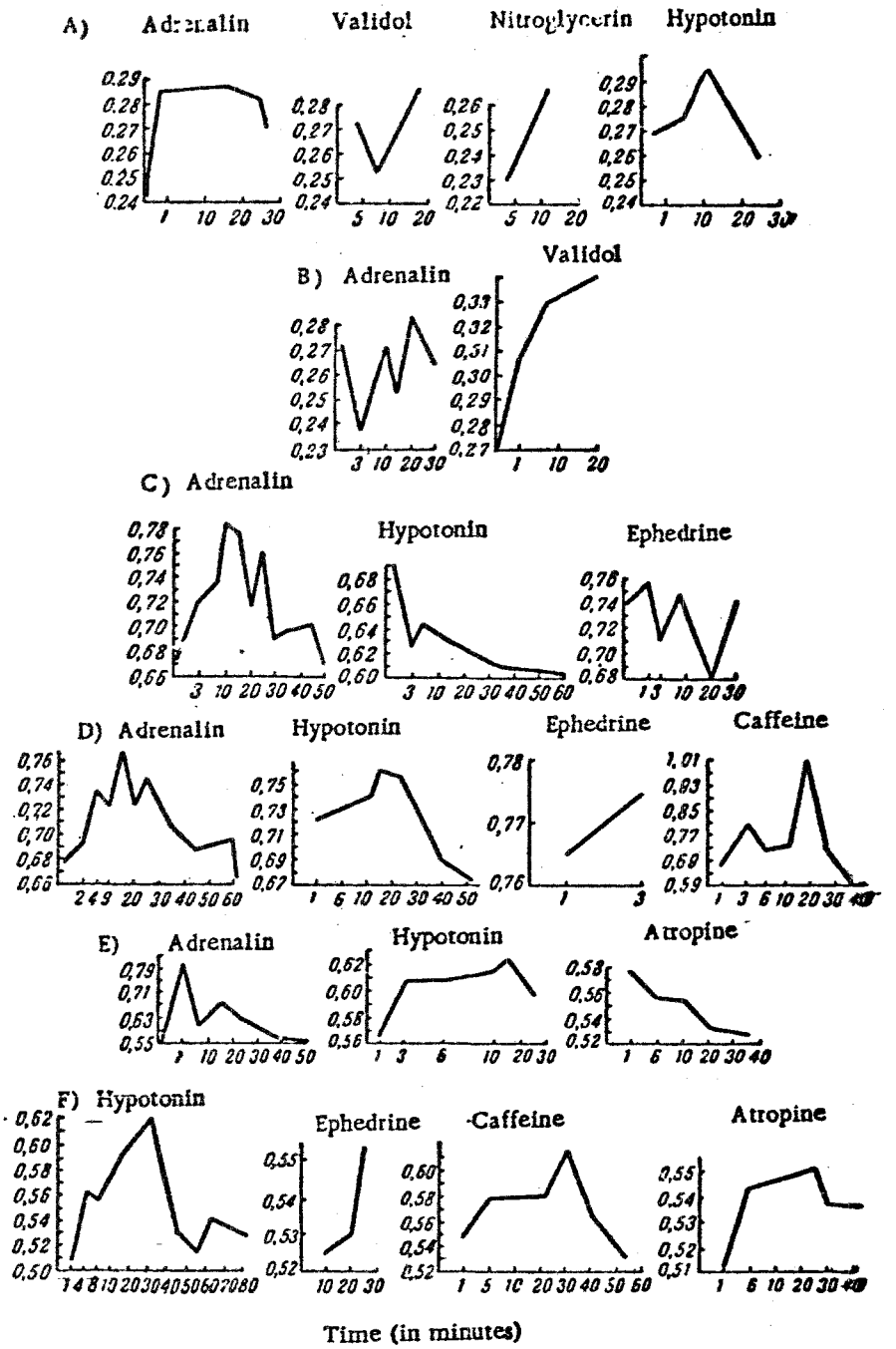


Fig. 1. Actions of various cardiovascular substances upon arterial net. Vertical figures (indicate width in cm of vessels) are magnified fourfold in comparison with actual size. A, B, C, D, E, and F – different experiments.

In one of the hypotonin experiments (Experiment C) additional introduction of adrenalin caused marked stenosis of the vessels within 3 minutes. Systole lengthened during this time from 0.20 to 0.25. During this experiment, P voltage increased, comparatively speaking, while R had a very small voltage. The height of both waves approached each other.

During the researches of N. P. Speransky, conducted in our laboratory, it was determined that hypotonin causes in dogs both in acute and chronic experiments when introduced intravenously and orally a marked diastolic drop (from 30 to 80 mm starting from original base), and persisting up to 2-5 hours and even longer.

In the control experiment (Figure 2,A) we twice introduced physiological saline intravenously in amounts of 0,8 and 1 cc. The ECG showed no change.

Direct observation of the net of vessels of the heart in a dog by means of prolonged kinescopy for 78 minutes has demonstrated that marked diameter variations can take place (dilation and contraction). Some substances produced marked fluctuations in the tone and diameter of the observed vessels. In this group is adrenalin (Experiment B, C, D), to a lesser degree ephedrine (Experiment C) and caffeine (Experiment D and F).

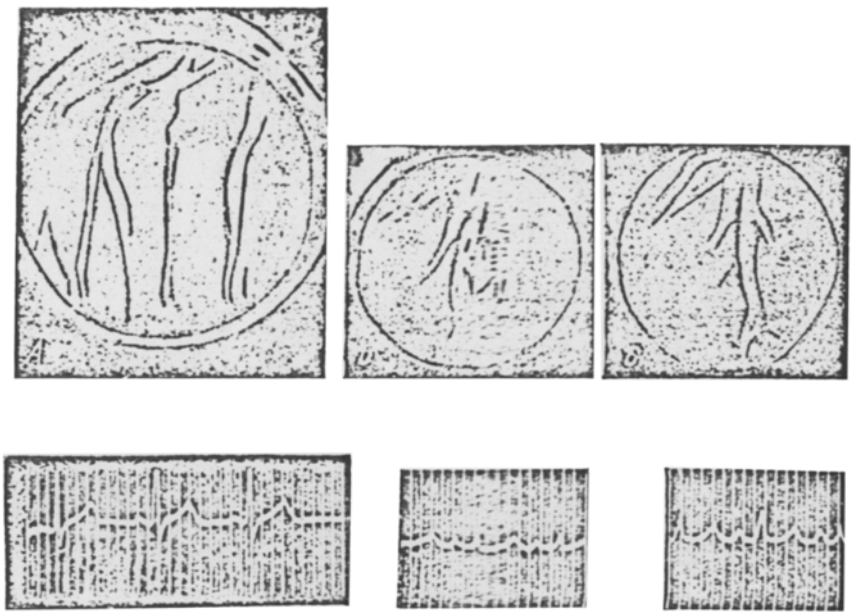

Fig. 2. Kinescopes and ECG. A) Experiment 11, 7/18/1955. Dog Swallow, wt. 17 kg. A large and five smaller branched arteries (magnification 1 and 1/2 x) ECG RR interval – 0.47 sec PR-0.1; QRS complex-0,05. Voltage of deflections: R-8 mm; P-1 mm; T-4 mm. Ensuing ECG did not vary from this; B and C – Experiment 6D, 4/14/1955 Dog Madam, wt. 8 kg, kinescope B – vessel net before introduction of hypotonin; kinescope C – vessels 10 minutes after intravenous injection of hypotonin solution, 6 mg/kg (0.5 cc 1% solution).

It is interesting to note that narrowing of the blood vessels can occur with the same substances that, in the majority of cases, produce dilation. This observation applies equally to almost all the substances studied: validol (Experiment A), hypotonin (Experiment C), atropine (Experiment E), ephedrine (Experiment C) and in some masure to adrenalin (Experiment B).

The condition of the vessels at the beginning of the experiment is of great importance in determining the experimental response.

Apparently, adrenalin has a tremendous influence on any reaction. For example, validol (Experiment A) caused a narrowing of the arteries after prior action by adrenalin, as was noted, similarly, with hypotonin (Experiment C) and with atropine (Experiment E).

Dilation of the arteries improved myocardial nourishment. Therefore, the ECG showed higher R and P waves. When the myocardial circulation was impeded as a result of contraction of the nutrient vessels, R was

diminished, systole was lengthened, and the T wave was flattened or inverted. These observations agree with the literature [2-11, 13].

Direct inspection of the blood vessel upon the heart surface is possible with use of kinescopic procedures and coordinated electrobiometric studies of the myocardium. This makes possible conclusions regarding the interrelationships between the character of arterial tone, myocardial blood supply, and the peculiarities of the electrical activity of the myocardium.

Changes in the blood vessels under the influence of drugs.

| Substance | Conditions of vessels[1] | | Observations | dose introduced of substances | Length of observation in minutes |
|---|---|---|---|---|---|
| | Widening | Narrowing | | | |
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[1] Figure indicates number of observations

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*In Russian.