# THE EFFECT OF PENTAMINE ON THE CARDIOVASCULAR SYSTEM OF DOGS UNDER VARIOUS CONDITIONS OF LONG-TERM EXPERIMENT

B. B. Voznesenskii

Department of Pathological Physiology (Head – Professor S. M. Pavlenko), First Moscow I. M. Sechenov Order of Lenin Medical Institute, Moscow

(Received April 11, 1957. Presented by Active Member Acad. Med. Sci. USSR V. V. Zakusov)

Pharmacologic investigations have shown pentamine* (analogue of the foreign preparation pendiomid) to be one of the most active of modern ganglion-blocking agents. According to I. M. Sharapov's data [1], pentamine exerts marked inhibitory influence on transmission of excitation in autonomic ganglia and lowers their sensitivity to certain pharmacologic substances. At the same time the reactivity of peripheral adrenergic elements is little altered. Pentamine has a definite hypotensive action but enhances pressor reactions to adrenalin. According to the same author, pentamine weakens reflex reactions associated with stimulation of the vagus and sciatic nerves and excitation of the carotid sinus mechanoreceptors. Experiments with cytisine showed that pentamine also diminished the reactivity of the adrenal medulla.

The present work is concerned with the study of the effect of pentamine on the cardiovascular system of dogs under ordinary conditions and against the background of marked arterial blood pressure and ECG changes elicited by conditioned stimuli.

## EXPERIMENTAL METHODS

The experiments were performed on 4 dogs, weighing 14-19 kg. Stereotyped motor-defensive conditioned reflexes with electrocutaneous reinforcement were established in all the dogs. The arterial blood pressure was determined in the common carotid artery externalized in a skin flap and records of the ECG were taken; both these determinations were carried out in the conditioned reflex chamber, before and after the experiment. Arterial pressure was determined with the dog standing in the special stand. Three standards leads were used for ECG recording. The reaction to adrenalin was studied in terms of changes in arterial blood pressure and ECG. Adrenalin in 1 : 40,000 dilution was injected into the popliteal vein in the dose of 0.5 ml. Arterial blood pressure and ECG were recorded at the moment of adrenalin injection and 1, 2 and 3 minutes after the injection. Pentamine was given into the popliteal vein, each dog receiving a dose of 1 mg/kg and of 5 mg/kg.

## EXPERIMENTAL RESULTS

Pentamine in the doses referred to produce no appreciable changes in the general condition of the dogs or in their behavior. The hypotensive effect in all cases was slight: the systolic and diastolic pressures dropped by an average of 10 mm Hg. In isolated experiments in which the arterial blood pressure exceeded the average normal values the hypotensive effect of 5 mg/kg pentamine was stronger: the pressure fell by 20-30 mm Hg (Fig. 1).

The ECG changes occurring under the influence of pentamine (1 and 5 mg/kg) were in all cases characterized, from the 2nd minute following the injection, by a sharp shortening of the R–R interval (tachycardia) and disappearance of sinus (respiratory) arrhythmia which was observed under ordinary conditions. The P–Q interval was, as a rule, shortened by 0.02-0.05 sec in all the dogs, the voltage of the P wave being increased. In most of the experiments pentamine caused diminution of the positive phase of the T-wave and increase in the T-wave

* Russian trade name.

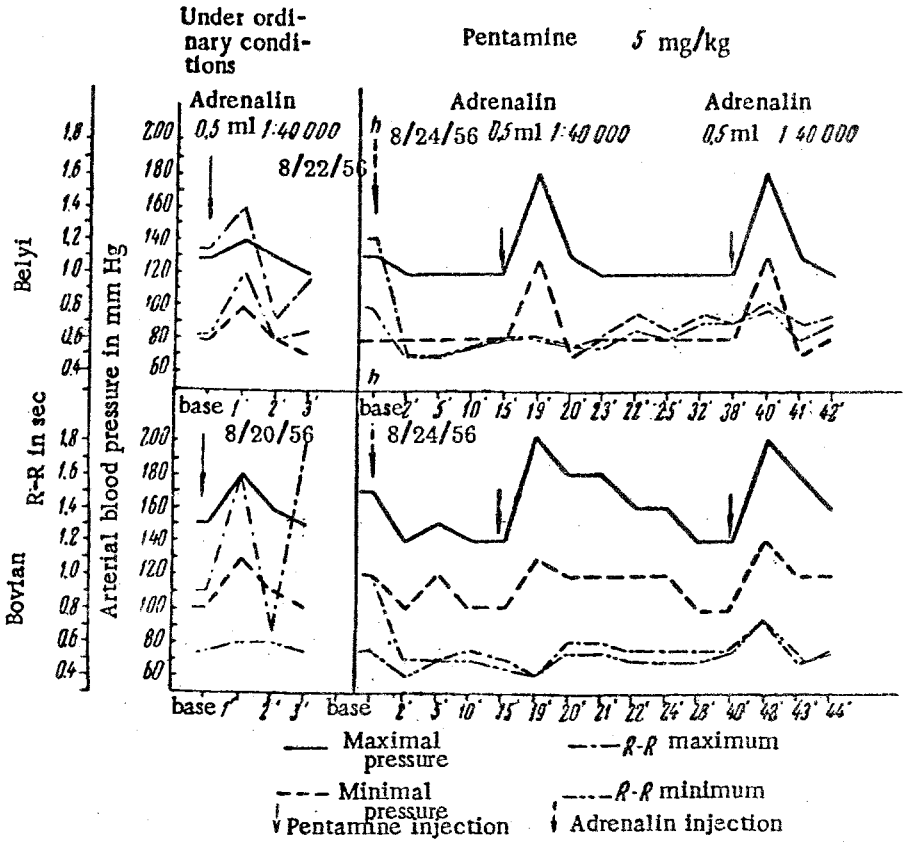


Fig. 1. Effect of pentamine (5 mg/kg) on arterial blood pressure, cardiac rhythm and sensitivity to adrenalin (0.5 ml, 1:40,000).

electronegativity. Injection of adrenalin against the background of pentamine produced more marked rise of blood pressure than under ordinary conditions (Fig. 1). The greatest effect was noted in the dogs Ryzhii and Tarzan which exhibited relatively high sensitivity to adrenalin in the initial period. Thus, while adrenalin, prior to injection of pentamine, produced a rise of blood pressure in Belyi, Bouian, Ryzhii and Tarzan amounting to 10/20, 30/30, 60/30, 40/30 mm Hg respectively, 15-20 minutes after pentamine injection (1 mg/kg) adrenalin produced rises of blood pressure of 30/30, 40/30, 70/60 and 60/50 mm Hg respectively. Repeat test with adrenalin 40-45 minutes after pentamine injection produced less effect, especially with respect to diastolic pressure. Pentamine given in the dose of 5 mg/kg elicited greater increase in sensitivity to adrenalin than that produced by a dose of 1 mg/kg.

Reaction to adrenalin as shown by ECG data following preliminary injection of pentamine (1 and 5 mg/kg) was distinguished from control experiments by the following features.

In all the dogs there was absence of vagus-pulse which usually appears during the 1st minute following injection of adrenalin, and enhancement of sinus arrhythmia. Furthermore, while under ordinary conditions adrenalin caused lengthening of the P–Q interval by 0.03-0.04 seconds (Belyi and Bouian), when pentamine was administered this lengthening was less marked and in some experiments there was even shortening of the P–Q interval by 0.01-0.02 seconds. In the case of the other 2 dogs (Ryzhii and Tarzan) adrenalin caused more pronounced shortening of the P–Q interval (by 0.03-0.04 seconds instead of 0.01-0.02 seconds) when given against the background of pentamine action than in control experiments.

Pentamine also exerted an influence on changes in voltage and direction of the T-wave following injection of adrenalin. When prior to pentamine injection adrenalin produced (in some dogs) diminution and disappearance of the negative phase of the T-wave and increase of the positive, against the background of pentamine this effect was less marked (in Bouian and Ryzhii). If, however, adrenalin produced, before injection of pentamine, diminution of the T-wave electropositivity and increased its negative phase, then following injection of pentamine

the reverse effect was seen: adrenalin, as a rule, increased the T-wave electropositivity.

After studying the effectiveness of the preparation and the distinctive features of its action with regard to the indices of the functional state of the cardiovascular system of dogs under ordinary experimental conditions, we

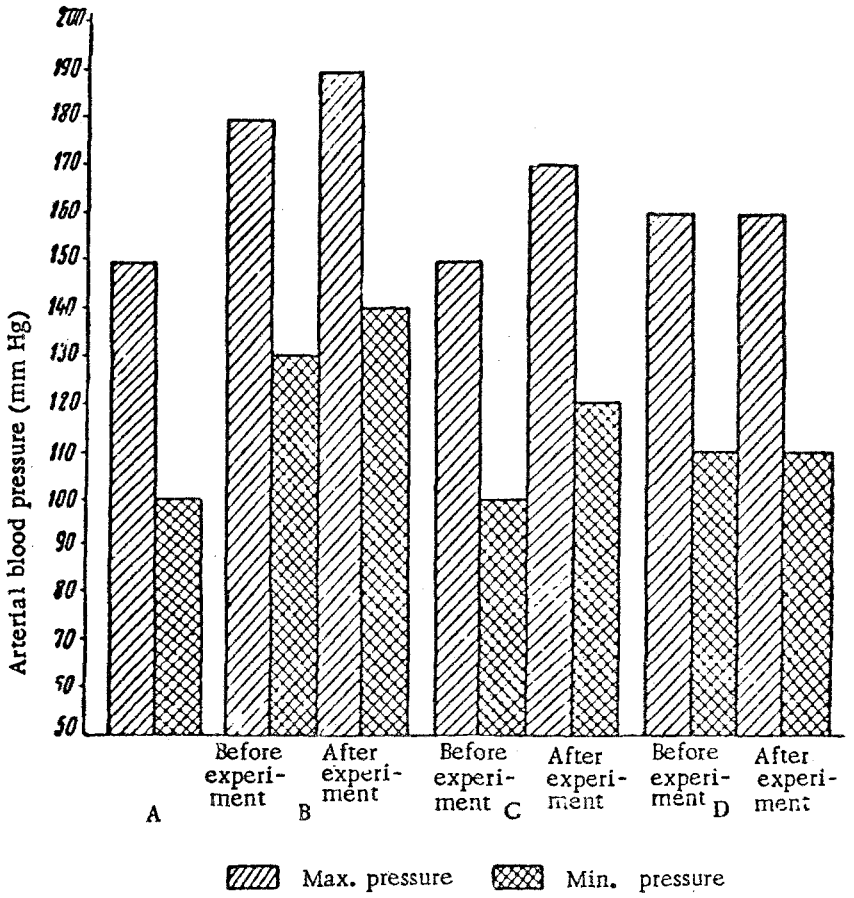


Fig. 2. Effect of pentamine (1 mg/kg and 5 mg/kg) on changes of arterial blood pressure in conditioned reflex chamber. Dog Bouian.
A) Average values of arterial blood pressure outside the chamber; B) changes in arterial blood pressure inside the chamber before and after experiment (without injection of pentamine); C) arterial blood pressures inside chamber after preliminary injection of pentamine in the dose 1 mg/kg; D) the same, dose of pentamine 5 mg/kg.

passed on to the study of the effect of pentamine on the circulatory apparatus against the background of conditioned stimuli. All the dogs had shown marked situational changes in arterial blood pressure and some of the ECG elements (changes in the P–Q and QRST intervals, marked sinus arrhythmia, changes in amplitude and direction of the T-wave) under the influence of functional factors ("confusion" etc.) impinging on them on being placed in the conditioned reflex chamber.

Situational changes in arterial blood pressure were expressed in definite hypertension which appeared immediately upon placing the dogs in the chamber. For example, when arterial blood pressure in the different dogs varied within the limits 120/70-170/120 mm Hg outside the conditioned reflex chamber, it was 150/110-190/140 mm Hg when the dogs were placed in the chamber prior to the experiment. After conditioned stimuli were applied the arterial blood pressure rose still higher, increasing by an average of 20-30 mm Hg.

Situational changes in the ECG consisted of a sharp shortening of the R–R interval (tachycardia), diminution up to complete disappearance of sinus arrhythmia, shortening of the P–Q and QRST intervals and changes in

Effect of Pentamine on ECG Changes in Conditioned Reflex Chamber, Dog Belyi

| Date | Experimental conditions | R–R | | P–Q | QRS | QRST | S–T | $T_2$ |
|---|---|---|---|---|---|---|---|---|
| | | Maximum | Minimum | | | | | |
| 7/22 1956 | Outside conditioned reflex chamber | 1.15 | 0.65 | 0.16 | 0.04 | 0.27 | elevated | +0.33 |
| 8/4 1956 | Inside conditioned reflex chamber (without administration of pentamine) before and | 0.55 | 0.50 | 0.15 | 0.03 | 0.23 | elevated | +0.30 |
| | after the experiment | 0.55 | 0.50 | 0.14 | 0.03 | 0.21 | " | +0.55 |
| 8/26 1956 | Inside conditioned reflex chamber 15 minutes after injection of pentamine (5 mg/kg) | 0.65 | 0.60 | 0.13 | 0.03 | 0.24 | elevated | +0.37 |
| | before the experiment | 0.70 | 0.65 | 0.12 | 0.03 | 0.23 | " | +0.25 |

Note: Intervals – in seconds; amplitudes of T-wave – in fractions of mv.

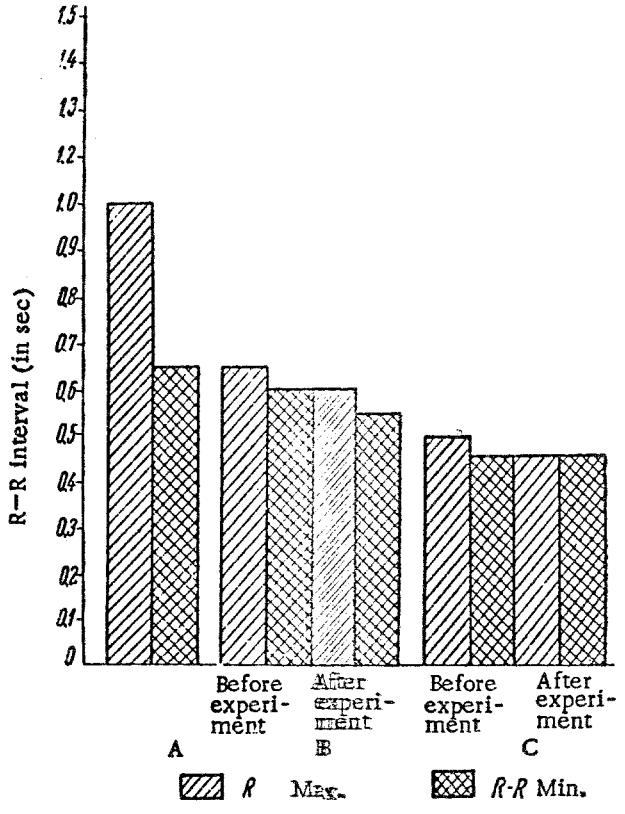


Fig. 3. Effect of pentamine (5 mg/kg) on changes of cardiac rhythm (according to ECG data) in conditioned reflex chamber; dog Bouian.
A) Average duration of the R–R interval outside the chamber; B) change in the R– R interval in the chamber before and after the experiment (without pentamine injection); C) change in R–R intervals in the chamber before and after experiment with preliminary administration of pentamine (5 mg/kg).

amplitude and direction of the T-wave. The use of conditioned signals caused enhancement of the ECG changes observed before the experiment.

The changes in arterial blood pressure and the ECG referred to above (occurring in the conditioned reflex chamber) were altered after preliminary (15-20 minutes before the experiment) injection of pentamine in doses of 1 mg/kg and 5 mg/kg in the following way. In all the dogs pentamine (1 mg/kg) abolished situational hypertension almost completely so that arterial blood pressure values observed in the chamber before the experiment but following preliminary administration of the preparation approached values usually found outside the chamber (Fig. 2). The use of conditioned stimuli, however, produced the same effect as in the control experiments, viz. a rise of blood pressure by 10-20 mm Hg; in other words, pentamine in the dose 1 mg/kg did not abolish completely the pressor influences associated with the use of conditioned stimuli. Pentamine in the dose 5 mg/kg abolished not only the situational hypertension but also, in the majority of cases, exerted a clear inhibitory influence on the development of the pressor effect associated with the use of conditioned stimuli.

Pentamine did not suppress the situational ECG changes which occurred inside the chamber. This is understandable, since it was shown earlier that the preparation itself produced in all the animals marked tachycardia, disappearance of sinus arrhythmia and shortening of the P–Q and QRST intervals.

The data obtained thus indicate that pentamine possesses slight hypotensive action and marked effect with respect to the ECG, causing tachycardia, disappearance of sinus (respiratory) arrhythmia, shortening of the P–Q and QRST intervals and alteration in the amplitude and direction of the T-wave. Pentamine potentiates the pressor effect of adrenalin and suppresses the vagus-pulse usually observed under the action of adrenalin. Pentamine in the dose of 1 mg/kg abolishes situational hypertension (in conditioned reflex chamber) and in the dose of 5 mg/kg also inhibits pressor effects connected with the use of conditioned stimuli.


## SUMMARY

It was established in experiments on 4 dogs that pentamine, introduced intravenously in doses of 1 mg per kg of body weight and 5 mg per kg has a slight hypotensive effect. On the other hand it has a pronounced influence on ECG, causing tachycardia, disappearance of sinus (respiratory) arrhythmia, shortening of P–Q and QRST waves, as well as the change of the amplitude and direction of T-wave. Pentamine increased the pressor effect of adrenalin and depressed the vagus pulse which was usually noted upon administration of adrenalin. Pentamine in the dose of 1 mg per kg removes situational hypertension (in conditioned reflex chamber). The dose of 5 mg per kg, besides giving the effect referred to, inhibits the pressor action connected with the use of conditioned stimuli.


## LITERATURE CITED


[1] I. M. Sharapov, Farmakol. i Toksikol., 18, No. 1, 8-13 (1955).

[2] H. I. Bein and R. Meier, Schweiz. med. Wschr., 1951, No. 19, pp. 446-450.