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EXPERIMENTAL PITUITRIN HYPERTENSION AND CORONARY INSUFFICIENCY IN MONKEYS

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It has been shown by A. A. Belous [1, 2] that daily intravenous injection of 0.5 ml of pituitrin for 13-15 days gives rise to persistent hypertension in dogs and rabbits. This author noted that pituitrin causes changes in cardiac activity. A comparison of the electrocardiograms taken before and after pituitrin treatment of dogs showed changes in the activity of the heart typical of coronary insufficiency. In rabbits, the electrocardiograms showed disturbances indicative of myocardial dystrophic change (arrhythmia, bradycardia, change in the electrical axis of the heart, lowered potentials).

Although experimental pituitrin hypertension in dogs and rabbits is not identical with the human condition, there are nevertheless grounds for believing that changes in the functioning of the endocrine glands, in particular the neurohypophysis, are of considerable importance in the pathogenesis of human hypertensive disease.

We thought it of great importance for the elucidation of the role of pituitrin in the causation of hypertensive disease to study the possibility of inducing pituitrin hypertension, and also the effects of pituitrin on the action of the heart of monkeys.

According to the reports of the Sukhumi Medicobiological Station [6, 7], spontaneous hypertension with symptoms of coronary insufficiency, resembling the picture seen in human hypertensive disease, is not infrequently encountered among monkeys maintained under artifical conditions. We attempted to establish whether pituitrin-induced hypertension with cardiac disturbances could be produced in monkeys, in the same way as in rabbits and dogs.

EXPERIMENTAL METHODS

The experimental animals consisted of 9 rhesus monkeys aged from $3\frac{1}{2}$ to 12 years, including 3 females and 6 males. Irrespective of age and weight all the monkeys were given one intravenous injection daily of 0.5-0.6 ml of pituitrin, for 18-22 days, except in one case (the monkey Karlik) in which only 12 injections were given when persistent hypertension set in. Blood pressure was measured daily in vessels of the forelimbs by means of a Riva-Rocci instrument, for 3 days before the course of injections, during the injection period, and after the injections had been discontinued. Electrocardiograms were taken over the whole of the observation period.

EXPERIMENTAL RESULTS

The initial blood pressure varied from 130/70 to 150/100 mm for 6 monkeys (Forum, Artam, Nil, Perepel, Vilya, Vanessa), and from 160/100 to 170/100 mm for 3 monkeys (Zlatka, Slepen', Karlik). Rise in blood pressure was observed after 4-8 injections, but it was not persistent. For this reason injections were continued

*In Russian.

until the blood pressure reached a constant high level. Daily measurement of blood pressure after discontinuance of pituitrin injections showed that persistent hypertension had developed in 7 monkeys (4 normotensives and 3 initially hypertensives), persisting over a 7-day period after the last injection. Hypertension did not develop in 2 monkeys (Vanessa and Perepel); Perepel exhibited elevated blood pressure during the injection period, with a return to the initial level immediately after they were discontinued. Subesequent successive measurments (2 and 7 months later) showed that blood pressure had returned to normal in 2 of the 7 hypertensive monkeys, while hypertension still persisted after a further 7 months in 5 monkeys (3 initially normotensive, 2 initially hypertensive). The object of the experiments on the initially hypertensive animals was to ascertain whether administration of pituitrin caused any further rise in pressure, and, what would be of even greater interest, whether it would affect cardiac activity. The variations in blood pressure of monkeys receiving pituitrin injections are presented in Figure 1.

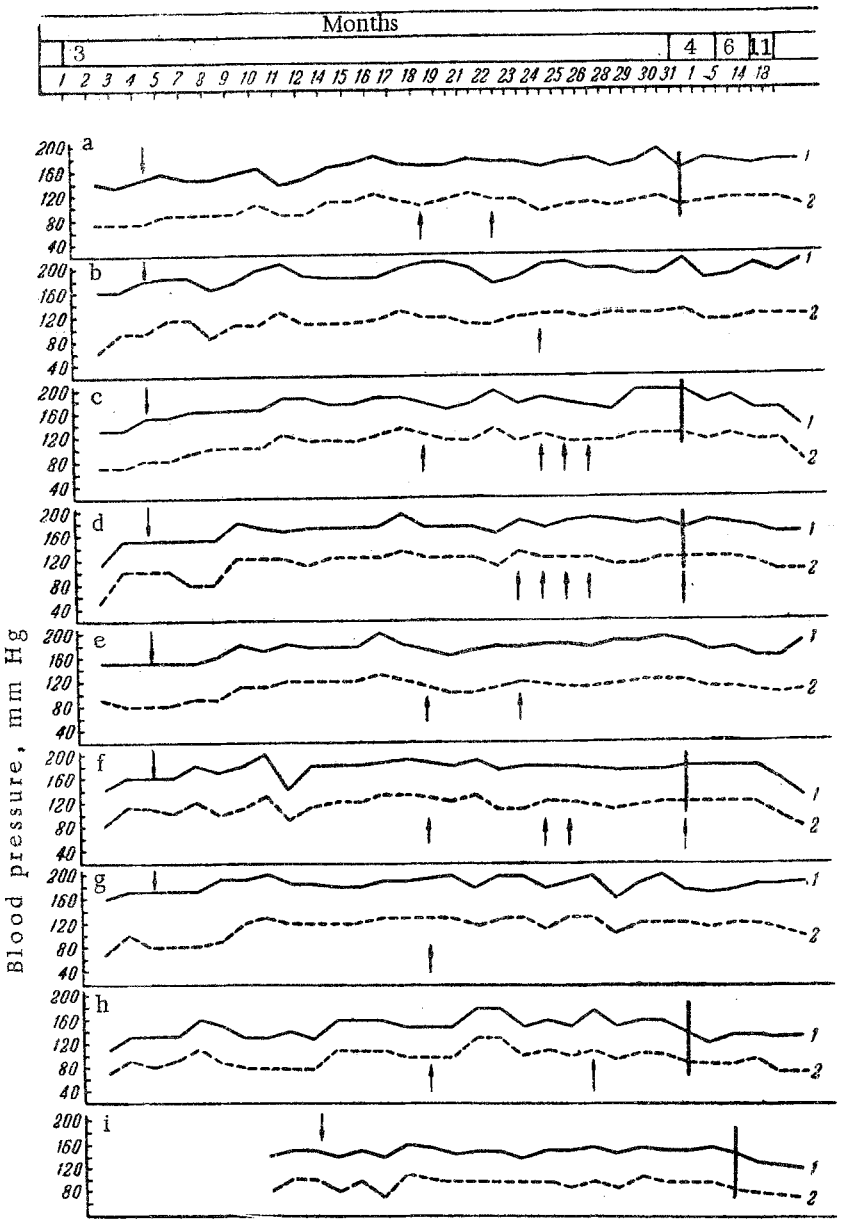

Fig 1. Variations in arterial pressure of monkeys receiving intravenous injections of pituitrin (March-November 1955). 1) aximum blood pressure; 2) minimum blood pressure; ↓ pituitrin injections commenced; vertical line – pituitrin injections discontinued; ↑ injection not given. Blood pressure curves for the monkeys: a) Forum 12 years old; b) Slepen 8 years; c) Nil 10 years; d) Vilya 5 years; e) Artam 5 years; f) Zlatka $7\frac{1}{2}$ years; g) Karlik 7 years; h) Perepel 6 months; Vanessa $7\frac{1}{2}$ years old.

The data of Figure 1 show that persistent hypertension developed in 7 of 9 injected monkeys.

Electrocardiographic study of the effects of pituitrin on the action of the heart showed the following: the preinjection of electrocardiograms showed no deviation from normal in 6 animals, and slight dystrophic myocardial changes in the other 3.

After daily pituitrin injections (for 15-26 days) electrocardiographic changes were seen, starting with the 11th-16th day in 6 animals, of the coronary insufficiency type in Nil, Forum, Karlik and Slepen (inversion of the T-wave with the standard and IV pectoral leads—(Fig. 2). Slepen displayed ventricular extrasystoles (Fig. 3).

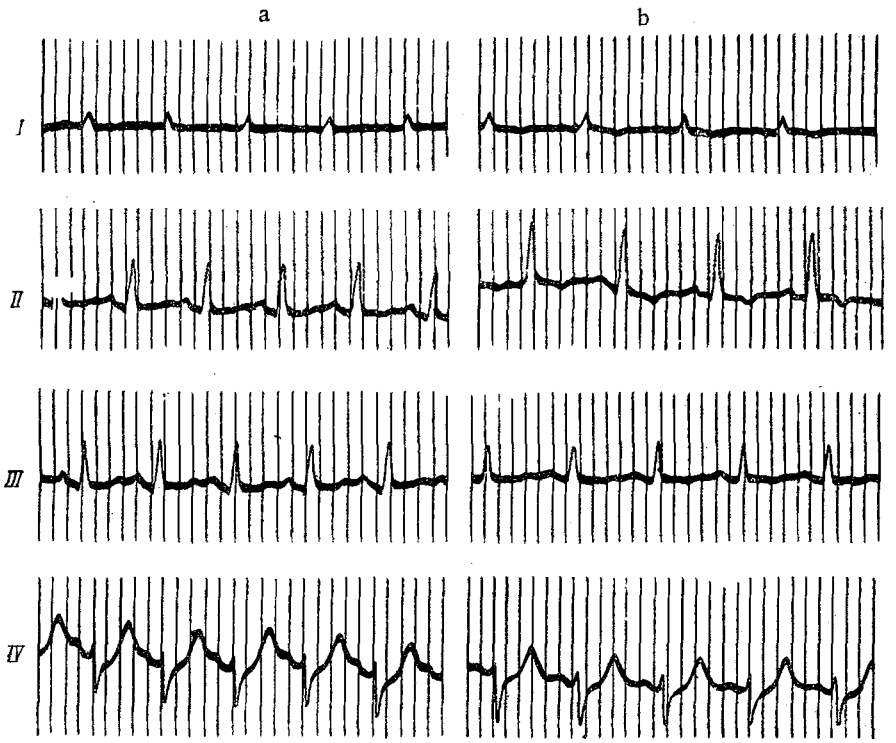

Fig. 2 Electrocardiograms for the monkey Forum a) Before, and b) after, introduction of pituitrin; Leads I, II, III, and IV.

Disturbances of cardiac activity appeared in one monkey (Vilya) on the 15th day; the E.C.G. shows auricular extrasystoles with lead III, and these were also seen 2 weeks after discontinuing the injections, with the IV pectoral lead. The monkey Perepel did not develop persistent hypertension, but only transient increase in pressure during the injection period; the electrocardiogram was indicative of dystrophic myocardial changes, viz., appearance of inverted T- and P-waves with standard lead III. The changes in the activity of the heart noted above persisted for a long time after pituitrin had been discontinued (over 2 to 7 months of observation). The ECG showed no deviations from the normal in 3 monkeys (Zlatka, Artam, and Vanessa).

DISCUSSION OF RESULTS

Our experiments show that it is possible, by means of intravenous injections of pituitrin, to induce hypertension in monkeys, as has been shown previously for dogs and rabbits [1, 2]. Our findings support the view advanced by numerous workers [3, 4, 5, 8, 9], that the endocrine glands may play a part in the pathogenesis of hypertensive disease, and in particular the hormones of the posterior lobe of the hypophysis. Our electrocardiographic studies showed that the changes in cardiac activity occurring after prolonged administration of pituitrin are of the type encountered in coronary insufficiency, and make their appearance about 5-7 days after the inception of hypertension.

It is not clear whether the cardiac disorders are ascribable to the direct action of pituitrin on the blood vessels and conducting system of the heart (inversion of the T-wave, and extrasystoles), or whether they are a

secondary consequence of the hypertension. Hypertension did not result in the monkey Perepel, which showed dystrophic myocardial changes (inverted T- and P-waves, in lead III). This is evidence that pituitrin can, independently of causing hypertension, exert a direct action on the coronaries, giving rise in the first place to dystrophic changes, from which result changes in cardiac activity of the type of coronary insufficiency.

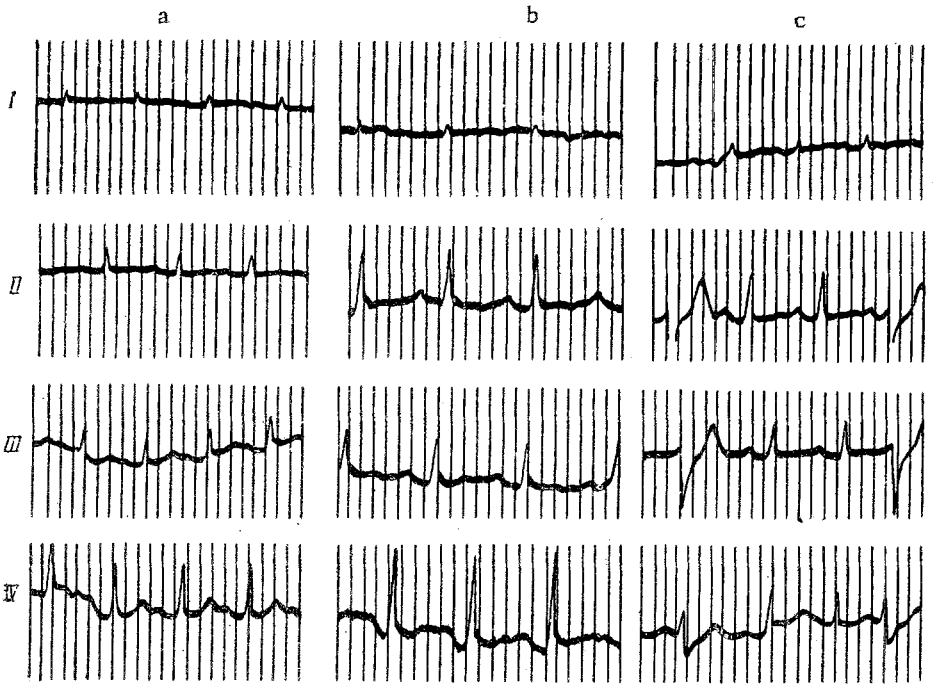

Fig. 3 Electrocardiograms for the monkey Slepen . a) Before injecting pituitrin, b) on the 14th day of injection, c) on the 5th day after discontinuing injections; Leads I, II, III, and IV.

Taking into account published evidence that hypertensive disease is frequently associated with coronary insufficiency, it may be concluded from our results that posterior pituitary hormones may, among other factors, be responsible for the origination of hypertension and cardiac disorders.

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