PHARMACOLOGY

CHANGES IN ARTERIOVENOUS ANASTOMOSES CAUSED BY THE ACTION OF CERTAIN DRUGS

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The aim of the present investigation was to study the function of arteriovenous anastomoses and in particular to discover the mechanism of regulation of changes in their lumina.

The state of arteriovenous anastomoses was determined by means of our modification of the method of microscopy of vessels in vivo, known in the literature as the method of "Clark's windows" (1931 [4]).

The essence of the method is that following careful dissection and excision of the cartilage from part of the ear of the rabbit a translucent layer of tissue is created, containing undamaged vessels with their innervation intact.

This area is enclosed in a transparent chamber made of organic glass* which permits observations to be made on the vessels by transmitted light for periods of weeks or months under the microscope.

We measured the diameter of the vessels by means of an ocular micrometer and the observations were recorded by means of a "Kolibri" microcamera [1].

Observations on the vessels in vivo made it possible to judge changes in their diameter, the character of contractions of the vascular wall and also the rate and direction of the blood flow.

Observations were made on 26 rabbits undergoing this form of operation. The duration of the observations on the vessels in the chambers varied from 3 weeks to $1\frac{1}{2}$ months. Each experiment lasted for one to 3-4 hours.

In order to study the mechanisms of regulation of the activity of the arteriovenous anastomoses, on the recommendation of S. V. Anichkov we used adrenalin, sympatholytin and hexonium, which interrupt the vegetative reflex arc at different points.

Experiments Using Adrenalin

In order to determine the character of the effect of stimulation of the sympathetic nerves on arteriovenous anastomoses adrenalin was used.

The effect of adrenalin on the arteriovenous anastomoses of the rabbit's ear has been studied by many workers [5, 6, 7]. According to all these writers adrenalin produced closure of the lumina of the arteriovenous anastomoses.

We injected rabbits subcutaneously with adrenalin in a dose of 0.3 to 1.1 mg per 1 kg body weight (22 experiments), usually using a dose of 1 mg.

As a rule the arteriovenous anastomoses reacted to the injection of adrenalin immediately. In the 2nd minute after injection their lumina began to diminish. The length of the period of closure of the anastomoses increased and their lumina rapidly disappeared completely. The arteriovenous anastomoses remained in a spastic state for a long time – for 2 hours and more after injection. The arterioles began to react to the injection of adrenalin somewhat later, and their diameter was reduced by an average of 70%.

* Plastic material used in the USSR.

The reaction of the venules to the injection of adrenalin was weaker than that of the arterioles – on the average the diameter of the venules was diminished by 45%.

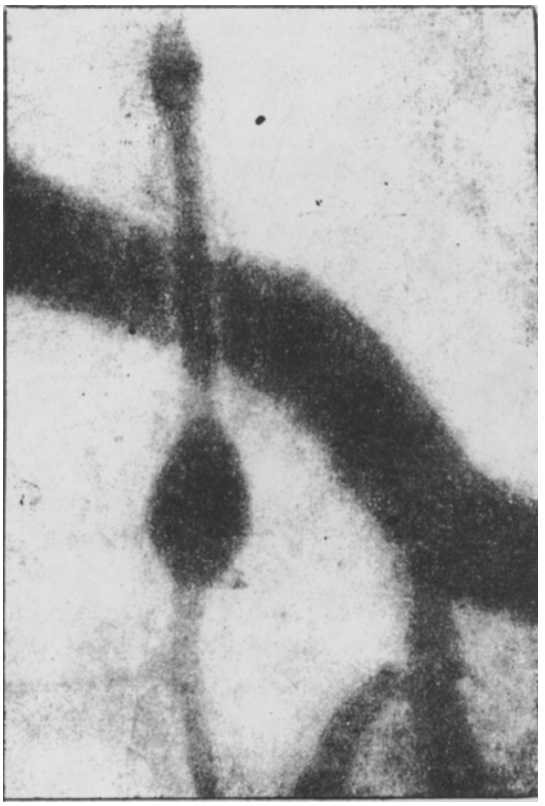

Fig. 1. Unequal contraction of the walls of the arteries of the rabbit's ear under the influence of adrenalin (0.1 mg/kg body weight). Microphotograph. Magnification: objective 8 ×, ocular 4 ×.

At the outset a slight, transient increase in the contractile activity of the arterioles could be observed, after which they became greatly constricted. In some cases the appearance of well-defined thickenings against a background of spastic contractions of the arterioles could be observed, and sometimes in the arteries also (Fig. 1). It must be emphasized that observations of this sort apply only to the arterial vessels, the lumen of the veins being constricted uniformly throughout their entire length after the injection of adrenalin. We were unable to find in the literature any description of observations of this sort.

The difference in the tone of the walls of the arterial vessels during the action of adrenalin is difficult to explain. We can only make the suggestion that adrenoreactive biochemical structures are unequally distributed throughout the arterial vessels.

Experiments Using Sympatholytin

Sympatholytin possesses a marked sympatholytic and adrenolytic action. The effects of sympatholytin are explained by its power to block the adrenoreactive biochemical structures of the tissues, with which the mediator of the sympathetic fibers and the adrenalin of the blood normally react [3].

We injected a 3% alcoholic solution of sympatholytin in 5 ml of physiological saline in a dose of 15-20 mg/kg body weight of the animals intravenously into the marginal vein of the rabbit's ear (11 experiments).

Within a few seconds of the injection of the sympatholytin solution the arteriovenous anastomoses which previously were closed were opened widely and simultaneously those which were already open were dilated still further.

As a rule the anastomoses remained maximally dilated (their diameter increased by 400-600%) for a period of $1\frac{1}{2}$ - 3 hours. The arteries and arterioles were considerably dilated – their diameter was increased 2 - $2\frac{1}{2}$ times, whereas the diameter of the venules increased by only $1\frac{1}{2}$ times. A clear acceleration of the blood flow through the vessels of the ear was also observed.

Simultaneously with the rapid and considerable dilatation of the arteries and arterioles very frequent pulsations appeared in their walls – over 200 pulsations in one minute, coinciding with the number of contractions of the heart. The amplitude of these pulsations usually did not exceed 10-15 μ.

Experiments Using Hexonium

In order to exclude pharmacologically the vasomotor neurone in the region of the synapses between the pre- and postganglionic sympathetic fibers we used hexonium which has the property of blockading vegetative ganglia, mainly sympathetic [2]. Hexonium was injected subcutaneously as a 4% aqueous solution (24 experiments).

It was discovered that hexonium in doses of 3-25 mg/kg body weight produces only slight acceleration of the blood flow and only in isolated experiments was slight dilatation of the anastomoses, arterioles and venules observed. Doses of hexonium from 30 mg/kg body weight and over resulted in obvious dilatation of the vessels. Administration of hexonium in a dose of 80 mg/kg body weight caused death of the animals.

The arteriovenous anastomoses and vessels of the ear began to dilate under the influence of hexonium after 2-8 minutes, reaching maximum dilation 12-27 minutes after the moment of injection of the drug. Gradually more and more of the arteriovenous anastomoses opened up; the lumina of those anastomoses which could be seen even before injection of hexonium increased considerably (Fig. 2). At the same time the anastomoses opened up the diameter of the arteries and arterioles increased (on the average by 130%), as did also that of the venous vessels (on the average by 80%).

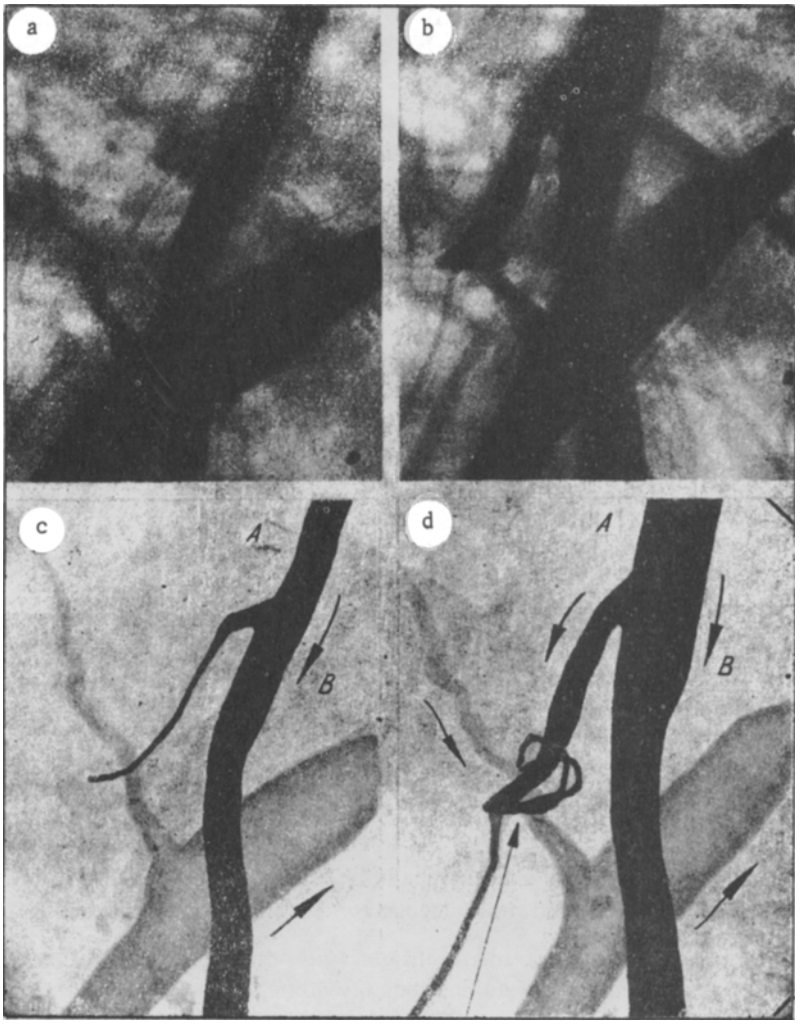

Fig. 2. The effect of hexonium on the arteriovenous anastomoses and vessels of the rabbit's ear.
a) Before injection of hexonium; b) 20 minutes after injection of hexonium (33 mg/kg); c and d) outlines of the microphotographs. The same magnification as in Fig. 1.

The duration of the vasodilatory action of hexonium in a dose of 33 mg/kg varied between 2½ and 4 hours.

The experiments using hexonium clearly showed that the resulting fall in the tonus of the sympathetic nerves was accompanied by opening up and dilatation of the arteriovenous anastomoses, and increase in the diameter of the arterial and venous vessels.

SUMMARY

The author studied the function of arteriovenous anastomoses with the aid of a modified method of direct microscopy of the rabbit's ear vessels in vivo. Changes of the diameter of vessels was evaluated with the aid of

the ocular micrometer and were registered microphotographically. Adrenalin, sympatholytin and hexonium were used for investigation of the mechanisms of regulation of activity of arteriovenous anastomoses. The results of observations allowed us to conclude that the main factor regulating the function of arteriovenous anastomoses is the increase or decrease of the tone of the sympathetic innervation.

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