PHYSIOLOGY

STUDY OF SYSTEMIC VASCULAR REACTIONS IN CATS BY THE METHOD OF COMPLETE ARTIFICIAL CIRCULATION

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The accurate detection and analysis of the systematic vascular component of complex reactions of the cardiovascular system are possible only by hemodynamic dissociation of the heart and lungs, on the one hand, and the whole of the systemic circulation on the other. An essential condition of such investigations is the maintenance of an adequate hemodynamics in the systemic circulation and the artificial oxygenation of all the venous blood, which can be done only by means of a complete artificial circulation.

The method of the complete artificial circulation has been used for analysis of the regulation of the circulation in experimental physiology only by a few workers, although their number continues to increase. Some authors have used the method of the complete artificial circulation to study reflex effects from the systemic vessels on the activity of the heart [1, 7], others to study reflexes from the heart on the tone of the systemic vessels [3, 6, 12, 14], a third group to study reflex relationships between the pulmonary and systemic circulations [13, 15] and, finally, a fourth group to study direct vascular effects in response to changes in the hemodynamics in the systemic circulation [11]. During the study of systemic vascular reactions, the investigators used the method of perfusion of the systemic circulation with a constant volume of blood [12, 14] or of perfusion under constant pressure with recording of the systemic blood flow [6]. Some authors [11] calculated the total peripheral resistance of the systemic circulation, using figures for the systemic arterial pressure and the systemic blood flow determined by means of flow meters.

Almost all the investigations mentioned above have been carried out on dogs. Only one report is known [9] of experiments in which a complete artificial circulation was used on cats.

The object of the present investigation was to develop a system of complete artificial circulation in cats, a convenient object for large-scale investigations in physiological, pathophysiological, and pharmacological laboratories.

The quantitative assessment of the systemic vascular reactions in artificial circulation conditions was carried out by the method of perfusion with a constant volume of blood (resistography) as developed by V. M. Khayutin and co-workers [4] for the study of regional vascular reactions.

The Perfusion Pump. For the separate but simultaneous perfusion of the systemic circulation and the heart (or lungs) we constructed with the help of A. P. Karyagin a two-channel perfusion pump of constant output, consisting of a "systemic" channel with an output of between 100 and 500 ml/min and a "cardiac" channel with an output of between 10 and 180 ml/min. In principle, the construction of this pump was the same as that used for the pump developed by V. M. Khayutin and co-workers [4]. The actual differences of construction were as follows: 1) instead of syringes of different volume, metal cylinders with stainless steel plunges were made, and their volume was made to correspond to the required output of the two channels of the pump; 2) hydraulic chambers containing blood were made from organic glass, and housed in one unit; 3) the two channels of the perfusion pump had common electromagnetic valves.

The system of electromagnetic valves, supplied by a direct current (80 v) produces a pulsating blood flow, with complete compression of both the afferent and efferent trunks of both channels of the pump, consisting below the values of short pieces of silicone-treated rubber, joined subsequently to polyethylene tubes. The working cycle of the valves is synchronized with the cycle of movement of the plungers by means of contact cams on the axis of the reducing gear of the electric motor, which regulate the time of operation of the contact system. The period of opening of each valve is 0.3 sec, and the period during which both valves are closed is 0.08 sec.

The rigid mechanical and hydraulic drive of the pump, the careful removal of air from the hydraulic system and the system containing the blood, the exclusion so far as possible of elastic elements, and the characteristics of

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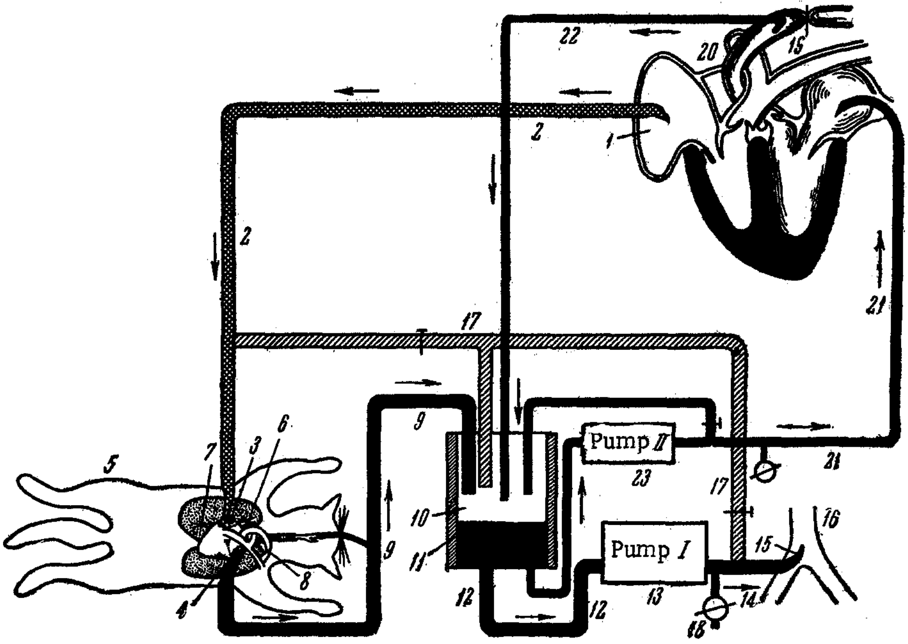

Fig. 1. Scheme for separate artificial systemic and cardiac circulation. Explanation in text.

the working cycle of the electromagnetic valves, as mentioned above, with complete compression of the tubes beneath them, create conditions ensuring stability of the output of the pump when the output resistance is changed. The loss of output of the pump does not exceed 5% when the pressure at the outlet of the pump changes from 0 to 100 mm Hg (for both channels).

Oxygenation of the Venous Blood. In the first stage of development of the artificial circulation system for cats, a foam-type oxygenator was used. At the present time, however, a biological oxygenator is used — the lungs of the donor cat previously used for obtaining the blood required for filling the artificial circulation system.

Homologous donor's lungs have been used by several workers to oxygenate the venous blood during the artificial circulation, and the following advantages of such lungs over artificial oxygenators have been described: 1) adequate oxygenation; 2) absence of trauma to the blood cells; 3) natural filtration of the blood; 4) ease and convenience of checking the oxygenation of the venous blood during controlled ventilation; 5) the small working volume required for filling.

The degree of saturation of the arterialized blood with oxygen is verified by means of a type PO-01 continuous flow oxyhemometer ("Biofizpribor"), the detector of which is placed along the course of the main arterial trunk of the perfusion pump. Ventilation of the donor's lungs is carried out with an air-oxygen mixture supplied to the donor's lungs by a DP-1 apparatus. In these circumstances the oxygen saturation of the arterialized blood is maintained at level of not less than 98% HbO_2.

A disadvantage of using the lungs of a dead animal as oxygenator is the possibility of edema, although this is not observed with normal ventilation supplied at the correct time (up to 10-12 cm water in inspiration), and a minimal (10-15 min) interval between the natural and artificial circulation and injection of heparine (2 mg/kg) into the donor before taking the blood. Not more than 15-20 min must elapse between death of the donor and using its lungs as oxygenator in the experiment.

The scheme of the artificial circulation is shown in Fig. 1.

All the venous blood of the recipient (the experimental animal), as a result of the difference in levels, passes through the polyvinyl chloride catheter (2) in the auricle of the right atrium (1)(external diameter 7 mm, internal 5 mm) into the auricle of the right atrium (3) of the donor (5), placed 48 cm below the level of the recipient. Both venae cavae (6, 7) and the ascending aorta of the donor are first ligated. After passing through the ventilated donor's lungs, the blood flows through the catheter (9) in the auricle of the left atrium (4) into the reservoir of arterialized blood (10), where it is warmed to 37.5° by means of a heat exchanger (11) connected to an ultrathermostat.

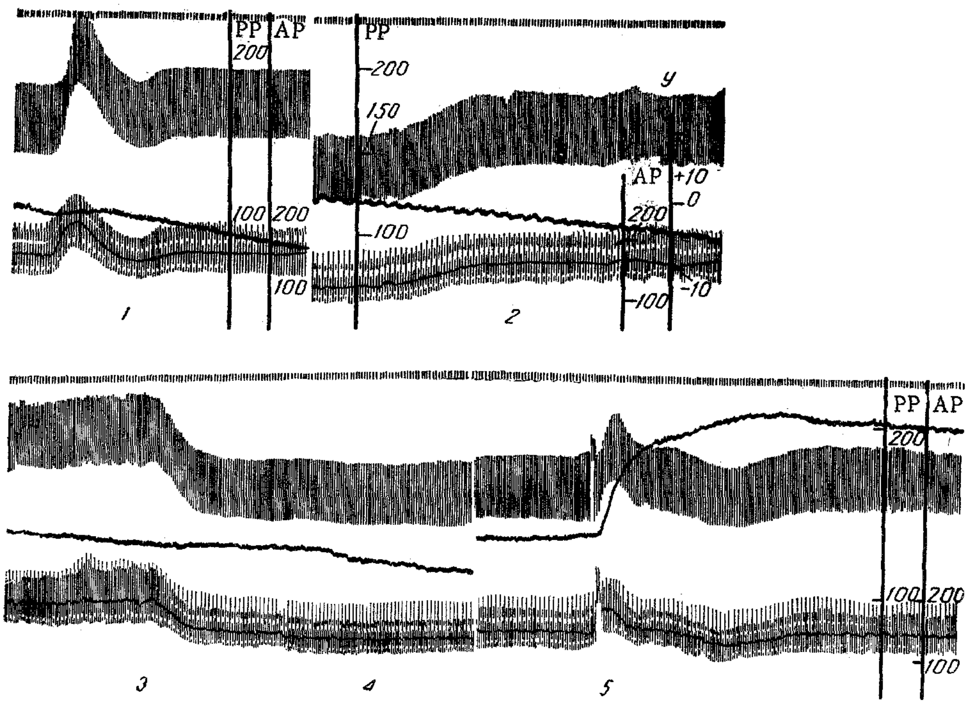

Fig. 2. Changes in the general perfusion pressure (resistogram) during electrical stimulation of the central end of the tibial nerve (1), compression of the common carotid artery (2), injection of hexamethonium (1 mg/kg) into the general perfusion system (3), electrical stimulation of the tibial nerve against the background of the action of hexamethonium (4), and injection of 1 ml of a 20% solution of sodium chloride into the general perfusion system (5). From top to bottom: time marker (1 sec); general perfusion pressure (PP); level of blood in the arterial reservoir; systemic arterial pressure (AP) in the common carotid artery.

The arterialized blood is drawn from the reservoir (10) through the main trunk (12) by the "systemic" channel of the perfusion pump (13), and having passed through the main trunk (14) and the metal cannula (15) into the common iliac artery (external diameter 2.2 mm, internal 2.1 mm) or into the abdominal aorta above the bifurcation (16; external diameter 3.2 mm, internal 3.1 mm). The overall perfusion pressure is recorded by an electromanometer (18).

Operating the Artificial Circulation. Before the beginning of the artificial circulation, the system of main trunks, the pump, and the reservoir of arterialized blood are filled with 175-200 ml heparinized donor's blood.

The experiment begins with operation of the "primary circulation" through the shunt (Fig. 1, 17) and the donor's lungs to produce maximal oxygen saturation of all the donor's blood in the artificial circulation system. After 5-7 min, the parallel circulation begins with the systemic pump working at a capacity equal to half the calculated minute volume (MV) for 1.5-2 min. Then, by compressing the ascending aorta (Fig. 1, 19) and pulmonary artery (20), the complete artificial circulation is established in the systemic channel and the output of the systemic pump is gradually increased to the calculated MV.

The MV is calculated from the weight of the recipient animal and data given in the literature for the magnitude of the MV in anesthetized cats [5], taking into account the influence of the open chest on the MV [8]. The MV of the artificial circulation varied from 180 to 280 ml (70-75 ml/kg/min) depending on the weight of the recipient.

As a rule pumping the calculated MV of blood into the arterial system leads to the creation of a general arterial pressure of 100-120 mm, thus demonstrating the adequacy of the hemodynamics in the systemic circulation and the absence of significant changes in vascular tone.

Particular attention is paid to constancy of the balance between the extra- and intracorporeal blood volume. An important factor affecting the maintenance of disturbance of equilibrium between these blood volumes is the resistance of blood vessels in the donor's lungs, determined by the aggregate size of their lumen. In addition, the state of tone of the systemic vessels at the beginning of the complete artificial circulation also plays an important role. If the initial tone is low, part of the extracorporeal blood volume at the beginning of perfusion passes into the systemic circulation.

Against the background of the artificial circulation, observations are kept on the state of the tendon and blinking reflexes. The systemic vascular reactions to electrical stimulation of the central end of the tibial nerve or to transient compression of one of the common carotid arteries are used as the index of excitability of the vasomotor center.

In artificial circulation conditions, in cats with the hearts and lungs excluded, the reflex excitability of the central nervous system can be maintained for between 1.5 and 3 h.

In the course of the complete artificial circulation, some degree of trauma to the blood cells is found. During perfusion for 1 h the erythrocyte count falls on the average by 400,000-500.000 per mm^3 (normal count in cats 7.5-8 million). Probably this slight degree of injury to the blood cells is the result of using the donor's lungs as oxygenator and using inert plastic tubes in the artificial circulation system.

Usually in the experiments recordings were made of the general perfusion pressure at the outlet of the systemic canal of the perfusion pump, as a function of the vascular resistance (with a stable systemic blood flow), and the mean systemic arterial pressure, using electromanometers constructed in the laboratory [2]. In some experiments, the level of the arterialized blood in the reservoir was recorded as an index of the systemic venous return.

If because of the experimental conditions, the activity of the heart has to be maintained, catheters are inserted into the auricle of the left atrium or into the ascending aorta, in the direction toward the heart, so that arterialized blood can be pumped into the left heart or into the coronary arteries respectively (Fig. 1, 21 and 22), by means of the second channel of the perfusion pump (23).

Examples of the systemic resistograms with different factors acting on the systemic blood vessels are given in Fig. 2.

The results of this experiment show that the application of a complete artificial circulation in cats, with a constant blood volume pumped into the systemic circulation, can be used to assess accurately the systemic vascular component of reactions of the circulatory apparatus to a wide range of influences.

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