followed by a rise, but it is noteworthy that after the fall of the instrument the rate of flow fell rapidly to below the initial level, as is shown in Figure 2. During another experimenton the effect of static loading the harness carrying the load accidentally slipped forward and downward, leading to an unexpected compression of the chest, which frightened the dog, causing it to struggle. Here,too, we observed a marked fall in the rate of flow of blood.

The effects on the rate of flow in the coronary artery of painful stimuli and of feeding remained the same over the whole period of observation following the operation.

One dog with an indwelling thermoelectrode died on the 42nd day after operation. Up to the day of its death the dog showed no external symptoms or signs of ill-health. Marked changes in the electrocardiogram were, however, seen two days before it died.

The above data illustrate the importance of the study of the physiology and pathology of the coronary circulation in unanesthetized animals. Under such conditions it is possible to follow changes in the blood supply of the heart due to various environmental factors, such as feeding, muscular exertion, etc.; such observations would not be possible under the conditions of a short experiment. Moreover, the experiments on painful stimuli gave clear evidence of the effect of the functional state of the central nervous system on the reaction of the coronary arteries during the experiment.

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REFLEX EFFECTS ON VASCULAR TONUS FROM CARDIAC MECHANORECEPTORS

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(Received June 24, 1955. Presented by V. N. Chernigovsky, Member Acad. Med. Sci. USSR)

One of the first indications of the existence of receptor functions of the myocardium and endocardium emerged from the so-called Bezold-Jarisch effect.

Bezold and Hirt [4] found in 1867 that injections of veratrine slowed the action of the heart. They interpreted this effect as being a cardiocardiac reflex. Similar effects were described by Jarisch and Henze [6] and by Richter and Schrockschnadel [9]. According to Jarisch, this reaction is effected through cardiac mechanoreceptors, the sensitivity of which is raised by veratrine; the effect involves stimulation of the vagus, with inhibition of sympathetic nerves.

Schaeffer [10] and others showed later that volleys of impulses from cardiac branches of the vagus are as a rule synchronous with contraction of the heart, but under the influence of veratrine the impulses become contінous (Jarisch and Zotterman [7]). The action of veratrine is exerted on receptors situated in the left ventricle (Schaeffer [10]).

A considerable number of papers have been published over the last few years, dealing with the study of the mechanisms of the nervous pathways of the Bezold-Jarisch reflex (see the detailed review by Dawes and Comroe [5]).

In his recent publications V. V. Frolkis [1] has shown that the activity of the heart involves the stimulation of myocardial receptors, and this significantly affects the excitability of the central nervous system.

This author showed in a second paper that during stimulation of a peripheral section of the vagus, disturbance in the rhythmicity of the heart caused stimulation of its interoceptive apparatus. This initiates the compensatory reaction, known as the phenomenon of "evasion" of vagus control by the heart [2].

Finally, Frolkis states in his last paper [3] that in experimental myocarditis the excitability of nerve centers is heightened, and that reflexes affecting the heart proceed more intensively even when the strengh of the stimulus is smaller.

However, in the majority of the above-cited papers the effects of factors exerted through the blood stream, and of reflexogenic vascular zones, were not fully excluded.

We have in the present research attempted to study the effects of reflex reactions originating in the heart on the blood vessels. In undertaking this research we were motivated both by theoretical concepts of the functional unity of the cardiovascular system and by clinical observations which gave evidence that stimulation of parts of the sensory apparatus of the heart affects the state of the vascular bed. In our experiments we excluded all possible connections between the heart and the blood vessels, other than nervous ones, and we applied adequate stimulators.

EXPERIMENTAL METHODS

In order to exclude all except reflex reactions between the heart and the vessels they were perfused separately, after being isolated (Figure 1).

A frog with an intact central nervous system was fixed rigidly to a special table. Both aortas were ligated, the right one closer to the heart, and the left one further from it. A Straub cannula was introduced into the centricle through the left aorta, below the ligature. The vessels draining into the venous sinus and the pulmonary arteries were ligated, taking care not to damage cardiac twigs of the vagus nerve.

Perfusion of the vessels was achieved through the right aortal arch, above the ligature isolating it from the heart. The Ringer solution was introduced into the vessels at constant pressure. The tonus of the vessels was assessed from the number of drops of perfusate emerging from the anterior abdominal vein over a period of 30 seconds.

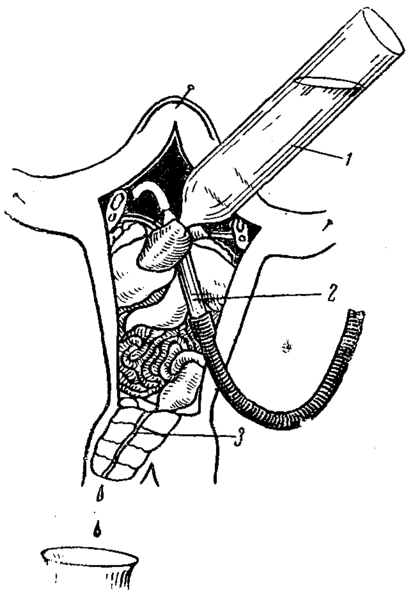

Fig. 1. Schematic representation of separate perfusion of the isolated heart and vascular system of a frog.
1) Straub cannula, introduced through the left aorta into a ventricle; 2) perfusing cannula inserted into the distal section of the severed right aorta, serving for the continuous perfusion of the vascular system with saline under constant pressure; 3) anterior abdominal vein.

Under these conditions changes in cardiac acitivity could not affect the vessels as a result of variations in the rate of flow of the fluid.

We had previously found that in the elucidation of the normal reflex interrelations between different parts of the cardiovascular system it is essential that adequate stimuli should be applied.

In our experiments stimulation was effected by changing the hydrostatic pressure in the Straub perfusion cannula. We placed 0.2 ml of Ringer solution in the cannula, and then added more solution up to 3 ml, thus raising intracardiac pressure by 15-25 mm of water. After a certain time the solution was sucked off down to the initial volume. The pressure was varied several times during each experiment, and in every case the number of drops emerging was registered.

Experiments on change in hydrostatic pressure in the right auricle, and in all parts of the heart simultaneously, were performed in an analogous way. Distention of the isolated auricle was achieved by introducing the cannula in one of two ways: a) through the anterior vena cava, and b) through a small aperture in the anterior wall of the ventricle.

EXPERIMENTAL RESULTS

After total isolation of the heart from the vascular system, raising of the hydrostatic pressure within a ventricle caused a diminution in the rate of flow of perfusate from the anterior abdominal vein, as compared with the initial rate. This is evidence of reflex raising of the tonus of the vessels. This effect was observed in 51 experiments, of a total of 55 in this series:

in 3	experiments	the	flow	fell	by	from	50 to 75 %
" 29	"	"	"	"	"	"	20 to 30 %
" 8	"	"	"	"	"	"	10 to 20 %
" 9	"	"	"	"	"	"	5 to 10 %

There was no change in rate of flow in 4 experiments.

We also observed a fall in the rate of flow of perfusate in 12 of 15 experiments involving raised hydrostatic pressure in the right auricle:

in 5	experiments	the	flow	fell	by	from	25 to 35 %
" 3	"	"	"	"	"	"	10 to 20 %
" 4	"	"	"	"	"	"	5 to 10 %

No change was found in 3 experiments.

Finally, raising the hydrostatic pressure in all the divisions of the heart caused a particularly large fall in the rate of flow of perfusate, in all the 14 experiments performed:

in 1	experiment	the	flow	fell	by	80 %
" 3	experiments	"	"	"	"	from 60 to 75%
" 9	"	"	"	"	"	" 40 to 50%
" 1	experiment	"	"	"	"	25 %

It should be noted that when all the chambers of the heart were distended simultaneously the tonus of the vessels rose very considerably.

Two cases are represented in Figure 2: a) change in flow rate when all parts of the heart are distended simultaneously, and b) when ventricle alone is distended.

It is evident that the effect is much greater in the former case than in the latter. The nature of the reaction is such as to preclude the possiblity of artifacts. Were the heart not completely isolated from the vessels the effect of elevation of pressure in the former would presumably be that a certain amount of saline would find its way from the heart to the vessels, and this should augment the flow from the anterior abdominal vein. This was shown to be the case in special experiments performed by us, in which ligation of the vessels was incomplete. In these experiments a certain amount of solution passed from the vessels to the heart, raising the level in the Straub cannula. The possibility of incomplete isolation of the vascular system, or of the intervention of any factors other than reflex ones, are excluded by the observation that the level remains constant in the Straub cannula, as well as by the nature of the reaction.

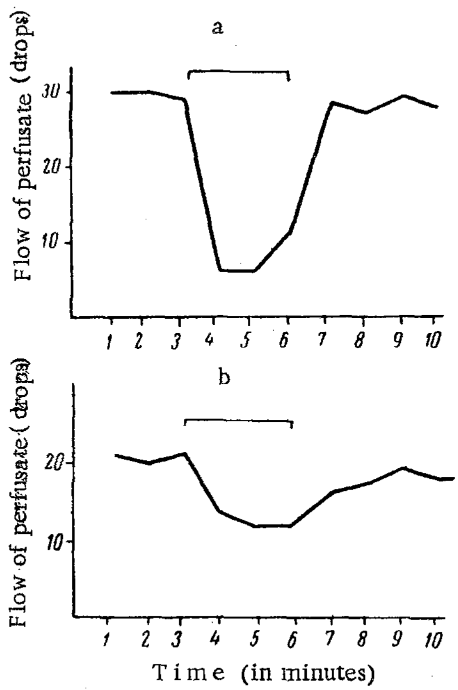

Fig. 2. Reflex changes in vascular tonus following raising of intracardiac pressure, under conditions of isolation of the heart from the vessles. a) simultaneous distention of all parts of the heart; disten ion of an isolated ventricle alone; ⌐¬ — pressure raised.

Our experiments show that the sensory structures of the heart are able to react to variations in pressure within its chambers. It is most probable that the receptors are sensitive not to pressure itself, but to distention of the muscular walls of the heart.

It may be concluded from our experiments that the most typical reaction to distention of the heart is raising of vascular tonus.

Although the conditions of our experiments excluded the possibility of any factors whatsoever other than reflex ones, we performed two series of experiments designed to confirm the reflex nature of the effects observed by us.

In the first series we destroyed the central nervous system of the frogs 30-45 minutes before the experiment, and then varied intracardiac pressure while perfusing the vascular system. In all the ten experiments of this series vascular tonus either remained steady, or else rose gradually and smoothly throughout the experiment, without any relation to variations in hydrostatic pressure within the heart.

In the second series of experiments we studied effects originating in the heart and acting on the vessels, under conditions of isolated perfusion, as before, but before and after section of the vagosympathetic pathways. In 19 of 25 experiments the tonus of the vessels diminished immediately after cutting the nerves, and the outflow of perfusate increased:

in 3 experiments by from 40 to 50 %
" 1 experiment " 30 %
" 10 experiments " from 10 to 20 %
" 5 " " " 5 to 10 %

There was no change in rate of flow in 4 experiments, and a diminution of 5-8% in 2 experiments.

Vascular tonus then returned to the initial level in all 25 experiments, and was not thereafter affected by varying intracardiac pressure (Figure 3).

It follows that the afferent pathways of the given cardiovascular reflex are contained in the vagosympathetic trunks. Interruption of the stream of impulses from the cardiac mechanoreceptors when the nerve trunks are severed leads in most cases to a lowering of the tonus of the vessels, i.e., the effect is the opposite of that observed when intracardiac pressure is raised. However, the nature of the effect produced by intracardial mechanoreceptors on vascular tonus is somewhat unexpected, and merits special consideration.

Enlargement of the heart under conditions of enhanced venous flow leads to a rise in arterial pressure, based on Starling's law, Bainbridge's reflex, and MacDowell's reflex. It may be supposed that under these conditions reflexes originating from cardiac mechanoreceptors should bring about a compensatory reaction, lowering excessive increase in arterial pressure. We, however, found a somewhat different effect, viz., to the raising of arterial pressure due to intensification of the action of the heart was superadded the effect due to increase in arterial tonus.

There is scarcely any need to point out that, as far as maintenance of constancy of arterial pressure is concerned, this reflex is pointless, and is in conflict with our basic concepts regarding these matters. One can only think that the rise in blood pressure associated with increased venous return, and proceeding in accordance with Starling's law and Bainbridge's reflex, is to some extent dependent on reflexes emanating from cardiac mechanoreceptors affecting vascular tonus, as described above.

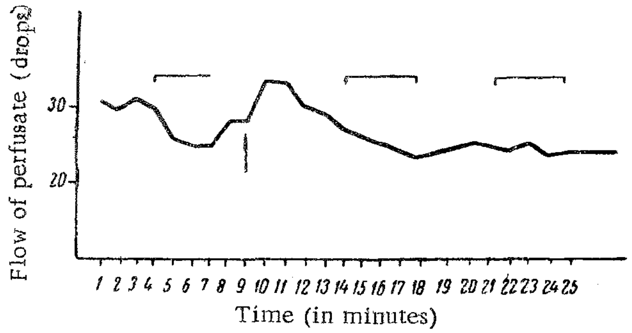

Fig. 3. Effect of section of the vagosympathetic trunks, under conditions of isolated perfusion of the heart and vessels, on reflexes from cardiac mechanoreceptors ⌐———¬ — pressure raised, ↑ vagotomy.

A consideration in greater detail of the conditions governing drainage of the venous system may assist in the comprehension of the role of the above-described reflexes, in the system of reactions regulating circulation of the blood. Accumulation of blood in the venous system must inevitably raise pressure within the veins, and distend their walls. The latter effect is associated, as was long ago shown by Bainbridge, with a sympathetic reaction from the heart, and, consequently, with intensification of transfer of blood from the veins to the arteries. Rise in venous pressure stimulates the work of the heart in other ways, first, according to Starling's law, and secondly by MacDowell's reflex. It thus appears that at least three different mechanisms are implicated in the regulation of transfer of blood from the venous to the arterial bed.

On closer consideration, however, redistribution of the blood between the venous and arterial systems cannot be thought to be a consequence of increase in cardiac output alone, since the latter leads not only to transfer of additional amounts of blood from the large veins to the large arteries, but also to acceleration of its flow from the arterioles through the capillaries to the venules, if the resistance of the vessels to the flow of blood remains unchanged. Discharge of blood from the venous system can only be effective if the enhanced flow of blood from the veins to the arteries (the cardiac component of the unloading reaction) is coupled with impedance of its return from the arteries to the veins (vascular component of the unloading reaction).

It may be thought that the reflex observed by us contributes to the achievement of this requirement.

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SIGNIFICANCE OF THE REFLEX FROM THE SUPERIOR VENA CAVA IN THE REGULATION OF BLOOD AND LYMPH CIRCULATION

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(Received March 16, 1956. Presented by V. N. Chernigovsky, Member Acad. Med. Sci. USSR)

The findings of a number of members of our Department (Z. G. Valeeva, D. I. Smirnov, K. V. Kovanov, G. H. Kotova), relating to functional connections between the lymphatic and blood vessels, have been presented in an earlier paper [1].

In the present paper we present some data obtained from further investigation and study of the significance of the reflex from the superior vena cava in the regulation of blood and lymph circulation.

We measured the pressure of lymph in the thoracic duct of a dog, using a mercury manometer, with simultaneous registration of arterial and venous (external jugular vein) pressure, with the object of ascertaining the strength of reflex contraction of the lymphatic vessels. In some cases we perfused the cervical lymphatic duct. Our experiments showed that intravenous injection of large volumes of physiological saline raises arterial pressure by 5-40 mm Hg, and venous pressure from 0-2 to 8-12 cm of water; at the same time the cervical lymphatic duct contracted to a state of complete spasm, and the pressure in the thoracic duct rose to 40-80 mm Hg (Figure 1).

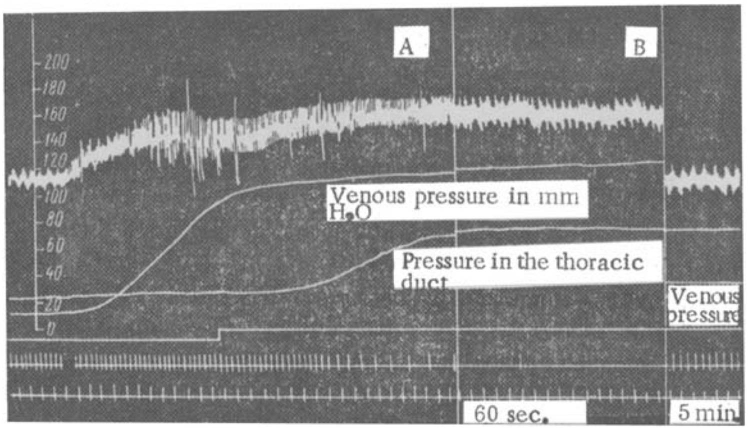

Fig. 1. Effect of intravenous injection of 400 ml of physiological saline on arterial and venous pressure and, pressure in the thoracic lymph duct, and on the tonus of the cervical lymph duct. A) Kymograph stopped for 1 minute; B) kymograph stopped for 6 minutes. Explanation of tracings, from above down: blood pressure in the carotid artery; lymph pressure in the thoracic duct, in mm Hg; venous pressure (right external jugular vein), in mm of water; flow of fluid through the cervical lymphatic duct (number of drops); time marker (5 seconds).