THE MYOCARDIUM AND THE HEMODYNAMICS DURING CARDIAC HYPERFUNCTION AND INSUFFICIENCY. REPORT 2. LOWERING OF THE RESISTANCE OF THE VASCULAR FIELD AS AN ECONOMIC COMPENSATORY FACTOR IN DISEASES OF THE CIRCULATORY SYSTEM

F. Z. Meerson, A. L. Mikoélyan, G. I. Markovskaya, and Yu. A. Vlasov

Institute of Normal and Pathological Physiology (Director, Active Member AMN SSSR V. V. Parin) of the USSR Academy of Medical Sciences and Institute of Experimental Biology and Medicine (Director, Professor E. N. Meshalkin) of the Siberian Division, USSR Academy of Sciences
(Presented by Active Member AMN SSSR V. V. Parin)
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When physical work is performed by a healthy organism, the minute volume of the heart may be increased many times over, not only as a result of an increase in the contractile function of the heart but also by a lowering of the resistance of the vascular field in consequence of a diminution of the tone of the smooth muscle of the arterioles. Because of this fact, a considerable minute volume may be achieved without an undue increase in the strain on the myocardium, and the cardiac hyperfunction mainly follows the lines of the isotonic (economic) variant.

From clinical experience it appears that in diseases of the cardiovascular system a decrease in the resistance of the vascular field plays an important role in the mechanism of economic compensation of the accompanying defects. However, the study of this aspect of compensation of diseases of the circulatory system is incomplete.

In the present research the role of the lowering of the vascular resistance in compensation was investigated in experimental aortic stenosis, producing a gradually progressive cardiac defect.

EXPERIMENTAL METHOD

Using a technique described previously [1], in 22 acute experiments on dogs a gradually progressive stenosis of the aortic orifice was produced, causing a graded constriction of the aortic orifice by 80-95% of its initial cross section. In all stages of stenosis the pressure in the left ventricle and aorta and also the minute volume of the heart were measured. The pressure was measured by means of a "Barovar" manometer manufactured by the firm "Alvar" and recorded on an ink-recording "Visograph" apparatus made by the same firm. The minute volume was determined by Fick's method. The total peripheral vascular resistance was calculated from the usual formula

$$R = 1332 \cdot \frac{P}{V},$$

where R is the total peripheral vascular resistance (in dynes · sec · cm^{-5}); 1332 the coefficient of conversion of pressure, expressed in mm Hg, into dynes/cm; and P is the mean pressure within the aorta (in mm Hg) and V the volume velocity of the blood flow (in ml/sec).

EXPERIMENTAL RESULTS

It will be apparent from Table 1 that as the aorta was constricted the maximal systolic pressure within the ventricle increased gradually, ultimately reaching 247 mm Hg, i.e., twice the initial value of 122 mm Hg. This change, a direct expression of the increase in the strength of the ventricular contractions, was combined with a gradual lowering of the maximal pressure within the aorta. The intra-aortic pressure fell as a result of the progressive stenosis from 104 to 47 mm Hg, i.e., by more than half. Consequently, the ventriculo-aortic pressure gradient rose from 18 to 200 mm Hg, i.e., more than ten-fold. This ten-fold increase in the ventriculo-aortic pressure gradient was a factor in the maintenance of the normal or subnormal minute volume of the heart, for even when the cross-sectional area of the aorta was reduced by 90-95%, the minute volume fell on the average to not less than 80% of normal.

TABLE 1. Changes in the Maximal Pressure in the Ventricle and Aorta, in the Ventriculo-Aortic Gradient and the Minute Volume (mean values for the whole group of experiments) Depending on the Degree of Stenosis of the Aortic Orifice

Criterion	Degree of constriction of cross section of aortic orifice (in % of initial area)							
	0	20—50	50—60	60—70	70—80	80—90	90—95	Stenosis removed
Maximal systolic pressure in left ventricle (in mm)	122	126	129	151	157	174	247	117
Maximal systolic pressure in aorta (in mm)	104	99	94	93	79	58	47	86
Ventriculo-aortic gradient (in mm)	18	27	35	58	78	116	200	31
Minute volume of the heart (in ml/min)	4 106	3 934	3 963	3 692	3 374	3 970	3 296	3 345

In this hemodynamic picture, typical of aortic stenosis, particular attention is drawn to the fact that the aortic pressure was halved while only a very small decrease took place in the minute volume of the heart. This change was a definite sign of a lowering of the peripheral vascular resistance.

Calculation of the peripheral vascular resistance showed that in the course of progressive aortic stenosis this index altered variously in different animals. In 16 experiments the resistance fell gradually as the degree of stenosis increased. The mean values characterizing this particular group of experiments are shown in Table 2.

It follows from the figures in Table 2 that with slight and moderate degrees of stenosis the resistance in the animals varied between 87 and 92% of normal; when the cross section of the aorta was closed by 70-80% it fell to 64.44% of normal, and finally, with the maximal degree of stenosis it fell to 23.45%, i.e., to less than one-quarter of the normal value.

The results of all the determinations of the resistance, demonstrating the individual variations, are shown in the graph (Fig. 1).

In the remaining six experiments the total peripheral vascular resistance was not lowered but, on the contrary, it was increased either immediately after the onset of stenosis (2 experiments) or when considerable degrees of stenosis were present (4 experiments).

When comparing these two groups of experiments it must be emphasized that if the lowering of the peripheral vascular resistance was considerable, the increase in the ventriculo-aortic gradient of pressures was largely the result of a fall in the pressure within the aorta, and only to a lesser degree of an increase in the pressure within the ventricle. As a result, the mobilization of the contractile function of the heart was relatively less pronounced: the strain on the myocardium and the total work of the heart did not reach an excessively high level. Compensation was due to a combination of cardiac and extracardiac factors, and was brought about in a sufficiently economic manner.

With an unchanged or increased peripheral vascular resistance, the increase in the ventriculo-aortic gradient resulted, conversely, from an increase mainly in the intraventricular pressure, i.e., from mobilization of the con-

TABLE 2. Changes in the Peripheral Vascular Resistance during Progressive Aortic Stenosis

Criterion	Degree of constriction of aortic orifice (in % of initial area)							
	0	20—50	50—60	60—70	70—80	80—90	90—95	Stenosis removed
Peripheral vascular resistance (in dynes · sec · cm^{-5})	2022,4	1760,7	1864,6	1779,7	1303,2	1115,3	474,24	3624,4
Peripheral vascular resistance (in % of initial value)	100	87,08	92,20	88,00	64,44	55,15	23,45	179,22

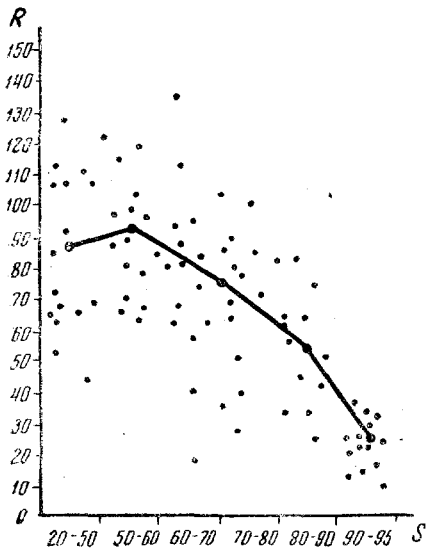

Fig. 1. Changes in the total peripheral vascular resistance in progressive aortic stenosis. R) Peripheral vascular resistance as a percentage of the initial level; S) degree of aortic stenosis as a percentage of the initial cross section.

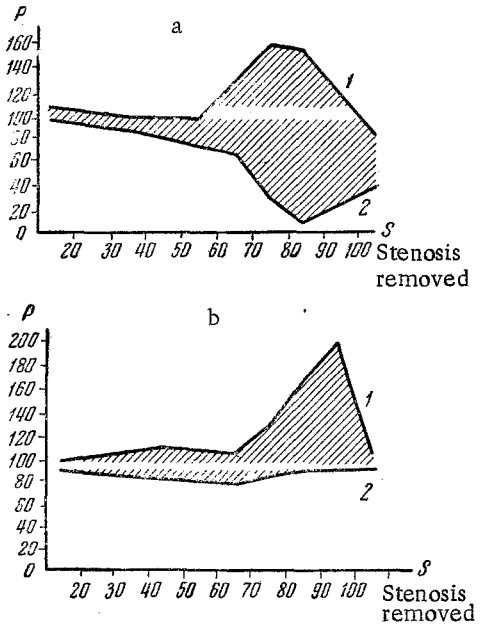

Fig. 2. Changes in the ventriculo-aortic gradient associated with a falling (a) and rising (b) peripheral vascular resistance during progressive aortic stenosis. P) Ventriculo-aortic pressure gradient (in mm Hg); S) degree of aortic stenosis as a percentage of the initial cross section.

tractile function of the heart – an increased strain on the myocardium and increased total work. Compensation was due mainly to the cardiac factor, i.e., it was associated with maximal utilization of the reserve powers of the heart.

From the curves in Fig. 2, a and b, we can compare the changes in the ventriculo-aortic gradient in experiment No. 12, in which the resistance fell and the minute volume of the heart remained at a subnormal level (a), and in experiment No. 21, where the resistance increased and the minute volume of the heart fell sharply (b). In experiment No. 12, with considerable degrees of stenosis, the increase in the ventriculo-aortic gradient to 150 mm was due to both an increase in the intraventricular pressure and a decrease in the intra-aortic pressure. In experiment No. 21 the ventriculo-aortic gradient was increased entirely as a result of an increase in the intraventricular pressure, and rose only to 100 mm.

It follows from the foregoing facts that in the development of progressive experimental aortic stenosis the lowering of the total peripheral vascular resistance is an important factor providing adequate compensation yet ensuring economic utilization of the reserve powers of the heart.

There is considerable factual evidence that the role of the peripheral vascular resistance in the compensation and decompensation of circulatory diseases is not limted to the special experimental situation we have been considering. Aortic stenosis in man is accompanied in most cases by hypotension, which was attributed in the past to a reduction in the minute volume of the heart. However, clinical physiological [7, 8] and experimental [2] investigations have shown that even in a high degree of aortic stenosis the minute volume of the heart remains normal, and the hypotension must, consequently, be attributed entirely to a fall in the peripheral vascular resistance. It may be supposed that the lowering of the diastolic pressure to 40 or 20 mm, or even to zero, observed in aortic incompetence is dependent not only on the reflux of blood through the defect in the semilunar valves, but also on the decrease in the peripheral vascular resistance. It is possible that these changes may play a part in the limitation of the diastolic reflux of blood from the aorta into the ventricle. In anemia, the mobilization of the circulatory function is an important compensatory factor and the minute volume of the heart may be doubled. However, this does not lead to elevation of the arterial pressure and, consequently, it is accompanied by a lowering of the peripheral vascular resistance. During the weeks, and even months, following myocardial infarction the arterial pressure of patients with hypertension is frequently normalized. This probably depends not only on a decrease in the minute volume of the heart, but also on a lowering of the peripheral vascular resistance.

In all such cases the lowering of the peripheral vascular resistance stands out as an important factor in economic compensation, preventing the wasteful expenditure of the energy-producing and plastic reserves of the heart and the premature exhaustion of the organ such as is observed after a long period of intensive, compensatory hyperfunction [3].

During the analysis of the mechanism lying at the basis of the lowering of the anteriolar muscle tone in compensatory hyperfunction of the heart, it must be borne in mind that in our experiments the lowering of the peripheral vascular resistance developed while the pressure within the aorta and carotid arteries was decreased and, consequently, the flow of impulses from the receptors of the aortic and carotid sinus zones was diminished. If the afferent impulses from these zones in fact determined the vascular tone, the resistance of the vascular field would not have been lowered but, on the contrary, it would have been increased, for when the flow of impulses from the pressure receptors of the aortic and carotid sinus zones is decreased, excitation of the vasoconstrictor sympathetic centers is observed as a rule. However, the resistance was lowered. The most probable receptor field from which an intensive flow of impulses could cause a lowering of the tone of the vasoconstrictor sympathetic innervation and a corresponding decrease in the peripheral vascular resistance is the receptor zone of the left ventricle, the pressure within which was greatly increased. Investigations by several workers [5, 6, 9] have shown that pressure and chemo-receptors are widely distributed in the myocardium of the left ventricle, and stimulation of these receptors by creating an increased pressure within the left ventricle or by injecting veratrine into the coronary vessels leads regularly to hypotension in the systemic circulation through the mechanism of a cardio-vascular reflex.

Hence, intensive compensatory hyperfunction of the heart may give rise to a reflex lowering of the peripheral vascular resistance, thereby putting into operation a new factor ensuring economic compensation. This situation corresponds to one envisaged [4], in which compensation after injury to the organism is achieved not only by a simple increase in the function of the compensating systems, but also by changes in the physiological working methods, guaranteeing the most economic utilization of the body reserves.

SUMMARY

During gradual reproduction of experimental aortic stenosis in dogs there occurs a considerable reduction of the general vascular resistance. This shift is clearly observed not only in stenosis of the aorta, it is an important compensatory factor maintaining the normal cardiac output in economic use of the myocardial reserves. A drop in vascular resistance during intensive cardiac hyperfunction may be due to the reflux from the receptors of the left ventricle to the arteriolar musculature.

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