STATIC CHARACTERISTICS OF THE BLOOD VESSELS OF THE KIDNEYS AND LIMBS

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The static characteristics of the link in the theory of automatic regulation define the relationship between the established values of input and output. The input value in the case of blood vessels is the frequency of the impulses of the constrictor fibers, and the output value is the degree of contraction of the smooth muscles. Theoretically the input value may vary within the range from complete inhibition of impulses to a slight decrease of their frequency, preceding the development of the "pessimal" effect. This range of changes in the frequency of the impulses determines the possible limits of contraction of the smooth muscles, i.e., the range of control by the hydraulic resistance of the vessels.

The contraction of the vessles in a resting state is maintained by "tonic" impulses of the constrictor fibers. However, we know that division of the splanchnic nerves does not increase the volume of the kidney [11]. On the basis of many reports indicating the absence of changes in the renal blood flow after denervation of the organ, the idea has developed that at "rest" the renal vessels are not subjected to the influence of constrictor impulses [21]. According to Pappenheimer's hypothesis [18], at "rest" the central structures generally speaking do not send constrictor impulses to the renal vessels. This worker accounts for the fact that impulses derived from constrictor fibers are constantly present in the renal nerves [4, 13, 20] by the acute conditions of the experiments. Also in an acute experiment, however, removal of the sympathetic innervation has a weaker dilator effect on the renal vessels than on the vessels of other organs. Blocking the sympathetic ganglia with tetamon lowers the resistance of the renal vessels on the average by 25.9%, compared with 61% in the case of the vessels of the hind-limb [6]. Meanwhile in acute cerebral anemia the resistance of the vessels of both organs increases to the same degree (by a factor of 2.6 [8]). On these grounds another hypothesis may be enunciated: it is not the intensity of the stream of tonic impulses that is different, but the magnitude of its effect on the vessels of the kidney and the hind-limb. The object of the present investigation is to verify this hypothesis by the examination of the static characteristics.

EXPERIMENTAL METHOD

In the first series of experiments on cats anesthetized with urethane (0.3 g/kg) and chloralose (0.05 g/kg), the resistance of the renal vessels was measured by the method of resistography [6]. Clotting of the blood was prevented with heparin. The splanchnic nerves were divided and one of them (on the same side as the perfused kidney) was stimulated with rectangular impulses (duration 8 msec, voltage 6-8 V). The responses of the renal vessels to stimuli of a frequency of 0.2, 0.6, 1, 2, 5, 10, 15, and 25 per second were recorded. In the second series of experiments the reactions of the vessels of the hind limb to stimulation of the sympathetic trunk, divided between the 4th and 5th lumbar ganglia, were recorded. Perfusion of the limb was carried out through the femoral artery, its profunda and lateral circumflex branches having been ligated. The perfusion pressure was established before division of the nerves to correspond to the mean arterial pressure of the animal. The supply of blood was not thereafter changed.

In the third series of experiments the effect of noradrenalin on the resistance of the vessels of the kidney and hind-limb was compared during simultaneous perfusion of the organs. Reflex influences on the vessels of the organs were eliminated by desympathization. The noradrenalin solutions were injected into the antebrachial cutaneous vein. The mean value of the reaction to a given frequency of stimulating impulses (or dose of noradrenalin) was found from the sum total of the absolute values of the increase in perfusion pressure (in mm Hg) in all the

experiments of the particular series, and expressed as a percentage of the maximal reaction. The degree of increase of the perfusion pressure at its maximal values was calculated in relation to the magnitude of the perfusion pressure before stimulation of the nerves.

EXPERIMENTAL RESULTS

The maximally effective frequency of the nervous impulses was the same for the vessels of both organs, namely 15 impulses per second (Fig. 1). In a few experiments the maximal effects took place at a frequency of 10 impulses per second. Identical figures for the limb vessels were obtained by Mellander [17]. Stimulation of the nerve trunks

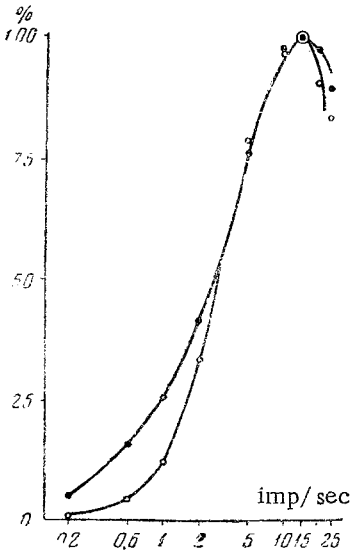

Fig. 1. Static characteristics of the renal vessels (white circles) and the vessels of the hind-limb (black circles). Along the axis of ordinates—increase in perfusion pressure (as a percentage of the maximal response, taken as 100); along the axis of abscissas—frequency of stimulation of the constrictor fibers (logarithmic scale). Mean results of 7 experiments on each organ.

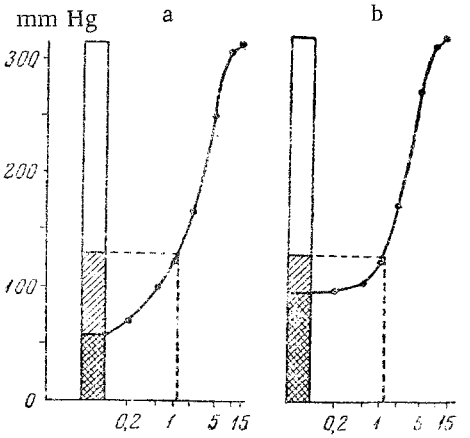

Fig. 2. Relationship between components of the resistance of the blood vessels. a) Of the hind-limb; b) of the kidney (the column diagrams on the left). The scale along the axis of ordinates is given in mm Hg. The static characteristics (on the right) are situated between the minimal and maximal gradients of the vasomotor component of the resistance.

accompanying the renal artery, according to Celander [10], does not produce constant, steady reactions of the renal vessels, and stimuli of a frequency below 2-3 impulses/sec are usually ineffective. Celander explains this by rapid injury to the nerves, and observes that even in relatively successful experiments not all the fibers innervating the renal vessels are stimulated.

Because of the foregoing considerations, we stimulated the splanchnic nerve. Impulses of a frequency of 15-30 per second will pass through the sympathetic ganglia without alteration of frequency [2, 8, 12]. It has been shown that the renal vessels are innervated only by the splanchnic nerve on the same side [9, 11]. Our experiments confirmed this finding. Finally, ligation of the adrenal veins had no effect on the reactions of the renal vessels. Special experiments showed that stimulation of the crossed sympathetic trunk between the 4th and 5th lumbar ganglia at a frequency of 10-15 impulses/sec increased the resistance of the limb vessels by only 7% (on the average), whereas stimulation of the ipsilateral trunk caused an increase of 261%. Hence, the reactions caused by electrical stimulation of the preganglionic trunks reflected the contraction of the smooth muscles of the vessels due to impulses in practically all the constrictor fibers.

Starting from a frequency of impulses of slightly more than 2 per second, the static characteristics of the vessels of the kidney and hind-limb were identical (Fig. 1). However, in the range of the lower frequencies they diverged. At a frequency of 1 per second the resistance of the hind-limb vessels increased on the average by 25.9% over the maximal, and the resistance of the renal vessels by 12.5%; at a frequency of 0.6 per second the corresponding

values were 16.2 and 4.4%, and at a frequency of 0.2 per second—5.4 and 1.2%. Hence impulses of low frequency constricted the renal vessels to a much lesser degree than the vessels of the hind-limb.

Let us examine how the difference in gradient of the initial part of the static characteristic curve affects the magnitude of the vasomotor component of the resistance of the blood vessels in a "resting" state. The diagrams of the relationship between the basic and basomotor components of the vascular resistance of the hind-limbs and kidney (Fig. 2) are constructed from the mean results of the experiments cited above [6, 7]. The cross-hatched part of the columns represents the basic component of the resistance, i.e., that part of the resistance of the blood vessels determined by structural and myogenic factors [15], and it persists after desympathization of the organ. The remaining part of the columns corresponds to the full value of the vasomotor component of the resistance from "zero" frequency of the nervous impulses to the maximally effective frequency. The stippled part of the columns thus represents that part of the vasomotor component of the resistance determined by the stream of impulses in the constrictor fibers in a "resting" state.

In acute cerebral anemia the resistance of the renal vessels is increased on the average by 260 ± 15%, and that of the hind-limb vessels by 262 ± 11% [7]. The resistance of the vessels of these organs corresponding to the maximally effective frequency of stimulation of the constrictor fibers rose on the average by 266 ± 22 and 261 ± 20%, respectively. The agreement between these four indices shows that in acute cerebral anemia the resistance of the vessels of both organs rises to the maximal possible limit.

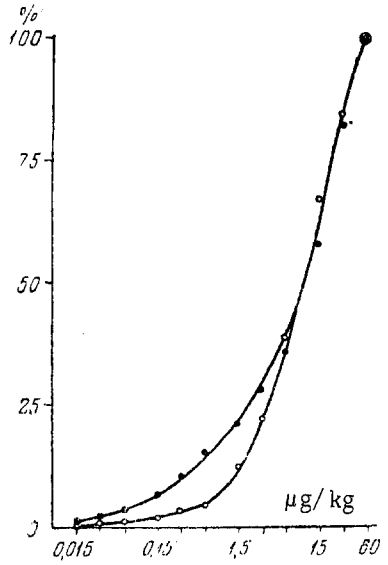

Fig. 3. Effect of noradrenalin on the vascular resistance of the hind-limb (black circles) and kidney (white circles). Along the axis of ordinates—increase in perfusion pressure (as a percentage of the maximal response, taken as 100); along the axis of abscissas—concentration in μg/kg body weight (logarithmic scale). Mean results of 5 experiments on the limb vessels and of 6 experiments on the renal vessels.

The value of the increase in the perfusion pressure in cerebral anemia, corresponding to the maximal possible neurogenic constriction of the blood vessels, determines the position of the maximum of the static characteristic curve. On the other hand, the level of the perfusion pressure after blocking the transmission of excitation through the ganglia, reflecting the state of the vessels in the absence of nervous impulses, determines the position of the zero point of the static characteristic curve. If the static characteristics are plotted between these limits and straight lines drawn to this curve from the level of the perfusion pressure in a "resting" state, it can be seen that these straight lines intersect the static characteristic curve at points corresponding to approximately the same frequency of impulses, namely slightly greater than 1 per second.

Hence, the vasomotor component of the resistance of the vessels of both organs in "resting" conditions is maintained by impulses with a frequency of about 1 per second. The same conclusion was reached by Folkow [14] in respect to the vessels of the skin and skeletal muscles. Direct measurement of the frequency of the tonic impulses in single fibers of the cervical sympathetic nerve also confirmed this conclusion [16]. The fact that the frequency of the "tonic" impulses in the constrictor fibers of different organs is the same is evidence against Pappenheimer's hypothesis regarding a specialized form of distribution of excitation in the individual parts of the vasoconstrictor system. The differences between the distribution of the vasomotor tone in "resting" conditions are due to differences in the pattern of the static characteristic curve of the vessels themselves. The absence of change in the blood flow after denervation of the kidney may be associated, however, not only with the relatively slight effect produced by the tonic impulses, but also with the ability of the renal vessels to control their own blood flow—a phenomenon most likely to be myogenic in origin [22].

How can we explain the differences in gradient of the initial parts of the static characteristic curves? The hind-limb vessels are capable of reacting to impulses in the constrictor fibers of lower frequencies than 0.2 per second (see Fig. 1). In some experiments slight constriction of the limb vessels could be observed during stimulation of the lumbar trunk at the rate of 1 impulse in 10 sec. However, the difference between the thresholds depending on the frequency of the impulses was fairly considerable. It is difficult, therefore, to ascribe the differences in the

gradient of the initial parts of the characteristic curve to, for example, the weaker powers of summation of the smooth muscles of the renal vessels. In fact, the "dose–effect" curves obtained in the experiments in which noradrenalin was given (Fig. 3) reproduced the distinctive features of the static characteristic curves of the corresponding organs. Although the initial part of the curve for the renal vessels was less steep, in this case the difference between the threshold concentrations was small. This indicates that the reason for the smaller effect of the low-frequency nervous impulses and of the small doses of noradrenalin on the renal vessels than on the limb vessels is the same. The difference disappeared as the renal vessels became more constricted.

Mathematical analysis of the factors responsible for the degree of the change in the resistance of the blood vessels in the course of their constriction forecasts that the increase in the gradient of the static characteristic curve must be determined by the decrease in the elasticity of the vessels [3]. During contraction of the smooth muscles the wall of the blood vessels thickens and thus becomes more rigid. This may also be one of the causes of the increased steepness of the static characteristic curve during contraction of the smooth muscles. Indirect support for this hypothesis is given by the decreased effectiveness of the constrictor impulses on the vessels of the functioning skeletal muscle [1, 19]. This may be associated with a decrease in the thickness of the walls of the arterioles relaxed by dilator metabolites. On the other hand, humoral agents causing the arterioles to contract must automatically potentiate the effect of the "tonic" constrictor impulses. This hypothesis requires confirmation, for a mechanism of this type may be concerned in the pathogenesis of diseases of the vascular tone.

SUMMARY

Static characteristics of the vessels of the kidney and extremities were studied in cats (relationship of hydraulic resistance to the frequency of constrictor impulses and noradrenalin doses). As established, the vasomotor component of the vascular "tone" of both organs is maintained by the impulses of the same mean frequency about 1/sec. However, the impulses of a relatively low frequency constrict the renal vessels less effectively than the vessels of extremities. The cause of this is the greater distensibility of the renal vessels and the sequence–an insignificant value of the neurogenic component of their "tone" at rest. Distensibility of the renal vessels reduces with contraction of the smooth muscles. The efficacy of constrictor impulses increases correspondingly. The realization of the nervous and humoral effects is determined by the biophysical properties of the vessels (relationship of the thickness of the wall to the radius-elasticity modulus).

LITERATURE CITED

1. A. M. Blinova and K. E. Serebryanik, In the book: The Regulation of Respiration, the Circulation, and Gas Exchange [in Russian], p. 42 (Moscow, 1948).
2. O. N. Zamyatina, Fiziol. zh. SSSR, 6, 687 (1961).
3. L. V. Nikitin and V. M. Khayutin, Fiziol. zh. SSSR, 8, 894 (1962).
4. Yu. L. Pines, Transactions of the I. P. Pavlov Institute of Physiology [in Russian], Vol. 6, p. 100 (Leningrad, 1957).
5. V. M. Khayutin, Fiziol. zh. SSSR, 7, 645 (1958).
6. V. M. Khayutin, Doklady Akad. Nauk SSSR 138, 488 (1961).
7. V. M. Khayutin, Doklady Akad. Nauk SSSR 138, 1473 (1961).
8. V. S. Sheveleva, Izv. Akad. Nauk SSSR, Seriya biol. 2, 94 (1956).
9. R. Burton-Opitz, Am. J. Physiol. 1916, v. 40, p. 437.
10. O. Celander, Acta physiol. scand. 1954, v. 32, Suppl. 116.
11. I. Cohnheim and Ch. Roy, Arch. path. Anat. 1883, Bd. 92, S. 424.
12. R. H. Eccles, J. Physiol. (London, 1955), v. 130, p. 572.
13. R. Engelhorn, Arch. exp. Path. Pharmak. 1957, Bd. 231, S. 219.
14. B. Folkow, Acta physiol. scand. 1952, v. 25, p. 49.
15. B. Folkow, In: Hypotensive Drugs (London, 1956), p. 163.
16. A. Iggo and M. Vogt, J. Physiol. (London, 1960), v. 150, p. 114.
17. S. Mellander, Acta physiol. scand. 1960, v. 50, suppl. 176.
18. J. R. Pappenheimer, Physiol. Rev. 1960, v. 40, suppl. 4, p. 35.
19. H. Rein, Ergebn. Physiol. 1931, Bd. 32, S. 28.
20. R. Sell, A. Erdellyi, and H. Schaefer, Pflüg. Arch. ges. Physiol. 1958, Bd. 267, S. 566.
21. H. W. Smith, The Kidney. Structure and Function in Health and Disease (New York, 1951).
22. W. H. Waugh and R. G. Shanks, Circulat. Res., 1960, v. 8, p. 871.