Role of the Nervous System in the Control of Vascular Tone

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It is well known that changes in vascular smooth muscle tone form the most powerful tool for the control of blood flow changes. Though it is generally agreed that the nervous factor is the most important one, it still is an open question how many, and which, mechanisms contribute to smooth muscle tone. An attempt will therefore be made to outline briefly the classical concepts of vascular control as contrasted to our present views, especially the relation of nervous control to other important mechanisms.

It is useful to define a baseline for activity of vascular smooth muscle. Such a baseline is best defined as the hemodynamic state created when vascular smooth muscles are at complete rest. This is most conveniently measured in terms of the flow resistance per 100 ml. of tissue at a normal distending and perfusing pressure, when a state of maximal vasodilation is induced. The level of vascular tone can then be quantitatively expressed as the ratio between the actual and the minimal flow resistance, just as one can estimate the state of activity of any isotonically contracting muscle from the extent of its active shortening. Of course this implies many simplifications but it is useful and easily performed.

This minimal flow resistance varies markedly in different tissues, which is not surprising since the respective vascular circuits can be expected to be structurally tailored to meet the extensive metabolic variations that are known to occur from one tissue to another. When expressed in terms of ml. flow/min./100 ml. of tissue the approximate values are, for example, for the myocardium 300 to 400 ml., for skeletal muscles 50 ml., for the brain 100 to 120 ml. In some tissues one finds values far higher than needed to satisfy maximal nutritional needs, e.g., in the skin, most glands, and the kidneys. Here, however, blood flow also serves other purposes: in the skin to allow for increases of heat loss and in glands and the kidneys to supply the raw materials necessary for secretion and urine formation.

The maximal blood flow capacity is, of course, only infrequently utilized; the vascular circuits are normally dynamically restricted by the vascular smooth muscles, the average activity level of which we call "vascular tone." This vascular tone implies the "blood flow reserve" of the tissues and it can be mobilized by smooth muscle inhibition. We come then to the basic questions in vascular regulation: exactly which mechanisms build up vascular tone and which factors are responsible for its inhibition?

These questions have been studied for more than 100 years, but we are far from the end of the story. Perhaps it is best first to outline the "classical" concepts. The main principles of vascular control were outlined by the pioneer studies of the nineteenth century that Bayliss2-4 coordinated to form a hypothesis, which was widely accepted for decades to follow. Being struck by the reciprocal control of the heart and the somatomotor neurons, he suggested that the blood vessels should also be under a reciprocal tonic nervous influence. The vasoconstrictor fibers and the hormones of the adrenal medulla should constitute the excitatory link under control of a vasoconstrictor center, in tonic reciprocal balance with a vasodilator center, controlling the vessels via sympathetic, parasympathetic, and dorsal root dilator fibers. This nervous control was thought to be fairly diffusely organized, executing mainly mass activation and inhibition patterns. It was also often assumed that what remained of vascular tone after cutting the
vasomotor nerves, should be mainly a consequence of constrictor agents in the blood. Lastly, though the vasodilatation in activated tissues was known to be mainly due to local factors ("vasodilator metabolites"), neurogenic vasodilator influences were often thought to form an important contribution. This gives in rough approximation the classical concept of blood vessel control, and we will next consider the question as to how the research of more recent years has changed these views.

It is now clear that the vasoconstrictor fibers form the sole efferent nervous link for tonic vascular control. In fact, the most frequent type of neurogenic vasodilatation is caused simply by inhibition of the prevailing activity of the medullary vasoconstrictor fiber center (VMC). There is no evidence of any tonically active, common vasodilator fiber center and the 3 vasodilator fiber types do definitely not form any functionally homogeneous group.5-7

It might be best to start by outlining the functional significance of the vasodilator fibers and return to the more important, the vasoconstrictor fibers, later. The sympathetic cholinergic vasodilator fibers are distributed only to the vessels of the skeletal muscles and possibly also to the coronary vessels. These fibers appear to be activated under circumstances in which they act in synergism with the vasoconstrictor fibers rather than being in reciprocal balance with them. Their highest representation is found in the vicinity of the motor cortex of the central nervous system, with relay stations in the anterior hypothalamus and in the mesencephalon, where the third order neurons bypass the VMC to make direct contact with the "final common path" in the lateral spinal horns, i.e., the preganglionic sympathetic neurons. On topical excitation of the hypothalamic integration station vasodilator fiber activation is combined with an excitation of vasoconstrictor fibers running to the skin, the gastrointestinal tract, and the spleen. In addition, activation of accelerator fibers to the heart and a hormone discharge from the adrenal medulla occurs. With very little shift in arterial pressure this autonomic activation pattern leads to a remarkable and instantaneous redistribution of the cardiac output to favor the skeletal muscles. When this region of the hypothalamus is topically stimulated in awake animals, a behavior typical of spontaneous rage or fear is induced, i.e., the autonomic pattern appears to be normally combined with a quite characteristic somatomotor activation pattern.8 Though these data are most suggestive, we cannot say that it is exactly known under which circumstances these fibers are normally activated. It is reasonable to assume activation in what Cannon called "emergency situations," simulating reactions of attack, defense, or flight. Furthermore, it is not excluded that these fibers might be more generally activated at the onset of muscular work, thus anticipating the needed increase of blood supply, though there is no experimental evidence. What is clear, however, is that the sympathetic vasodilator fibers are not engaged in the tonic control of the blood pressure as exercised reflexly from the different sets of cardiovascular proprioceptors.

The parasympathetic vasodilator fibers were previously thought to be widely distributed, for instance, in the gastrointestinal tract. It now seems that the majority of the so-called parasympathetic vasodilator fibers are not specific dilator fibers. On stimulation of the parasympathetic supply of the salivary glands, for instance, there is a release of a proteolytic enzyme, which splits off a polypeptide from normally present proteins in the tissue fluid.9 This polypeptide, often called bradykinin, is closely related to, or even identical with, pancreatic kallikrein, described thirty years ago, which also has a profound vasodilator action.10 It appears likely that a similar substance is released also from other activated gastrointestinal glands, and bradykinin is definitely released from the sympathetically innervated sweat glands, explaining the intensified cutaneous vasodilatation occurring when sweat production starts.11

The remaining specific parasympathetic vasodilator fibers appear to be those running to the pial vessels and the external genital
organs. Virtually nothing is known about the functional significance of the first-mentioned type going to the pia; they might, for instance, be activated in arousal stimulations from the reticular formation, thus contributing to increasing cortical blood flow. If so, they are not unrelated to the sympathetic vasodilator fibers with respect to the circumstances that excite them. But this is only speculation, and one feels more certain about the functional significance of the vasodilator fibers to the external genital organs.

The dorsal root vasodilator fibers, which Bayliss thought to convey efferent vasodilator impulses, are truly afferent fibers with no normal efferent function. It is known that the peripheral ramifications of pain fibers form an axon reflex arrangement with the adjacent blood vessels, responsible for the "flare" or "triple response." In all probability dorsal root vasodilatation is simply due to the antidromic activation of this pain fiber axon reflex arrangement. On antidromic excitation the stimulation strength has to be increased enough to excite also the C-fiber group before vasodilatation appears. The majority of the pain fibers belong to the C-fiber group and are distributed to superficial tissues such as the skin and certain mucous membranes. It is only within these tissues that any significant vasodilatation is obtained on dorsal root stimulation. An arrangement of this type must be of some value as a local defense mechanism against harmful stimuli, since regional blood flow is automatically increased as soon as pain fibers are excited. Since such fibers are also activated when the skin is chilled more intensely, it is not surprising that the axon reflex mechanisms appear to form one of the factors that are responsible of cold vasodilatation in the skin.

It is evident that these 3 sets of vasodilator fibers are neither tonically active, nor do they form any homogeneous group, but are specially engaged only under quite specific circumstances. The steady tonic neurogenic adjustment of the vascular bed is, as mentioned, exercised only by the vasoconstrictor fibers, and are engaged in practically any sort of cardiovascular adjustment, which make them the most important vasomotor fiber type. This does not mean, however, that they are the only important factor for the establishment of vascular tone. When they are regionally blocked, there remains in many tissues a marked vascular tone that we can call basal tone. For instance, in resting skeletal muscles blood is normally around 3 to 5 ml per 100 ml of tissue per minute, increasing to roughly twice the value on regional vasoconstrictor fiber block. It can, however, be increased another 4 to 6 times, up to about 50 ml, in muscular work. This implies a pronounced basal tone in this tissue. This is also the case in many other tissues, e.g., the myocardium and the brain; after elimination of all possible vasoconstrictor fibers to these tissues their vessels still maintain a considerable tone, though it is promptly inhibited by increased tissue activity. As a contrast to this, vessels like the cutaneous arteriovenous anastomoses become practically maximally dilated as soon as their constrictor fibers are cut, provided that the organism is in a "resting" equilibrium without any significant reflex increase of the hormone output from the adrenal medulla.

What is then the background of this basal vascular tone, which in some areas is so pronounced, in others moderate, and in still others practically absent? If it were due to blood-borne vasoconstrictor substances one would expect that the vessels with high basal tone should be more sensitive to such factors than, e.g., the cutaneous arteriovenous anastomoses. Exactly the opposite is in fact the case; for example, the vessels of the skeletal muscles are definitely less sensitive to all known biogenic vasoconstrictor substances than are the cutaneous arteriovenous anastomoses, which respond to exceedingly low blood concentrations. From these simple observations one can conclude firstly that basal vascular tone must be of an essentially local origin, secondly that in the normal resting organism the blood concentration of vasoconstrictor agents is fairly negligible. In fact, normally the blood concentration of the hor-
monal component of the sympatho-adrenal system exerts more significant excitatory effects on heart and the blood vessels only episodically and are then generally overshadowed by the direct sympathetic innervation. With exception of such episodic conditions and some pathophysiologic circumstances, as when angiotension is released via renin production, there is no evidence of functionally significant concentrations of vasoexcitor substances in the blood.

There is, on the other hand, good evidence that vascular smooth muscle cells, especially those of the smallest vessels, adjacent to the capillaries, show a rhythmic inherent activity, justifying the term myogenic automaticity. This is a well-known phenomenon in some other types of smooth muscles, but it is in some specialized types virtually absent, as in the intrinsic eye muscles. A myogenic activity will, of course, be profoundly influenced by external factors, but the essential point is that it is not basically a matter of any extrinsic excitatory influence, rather it is dependent on a normal environment, as are all forms of cellular activity. If great numbers of vascular smooth muscle cells show rhythmic but unsynchronized contractions, this will create a "vascular tone," and it is reasonable to assume that this is the very background of what has here been called basal tone. The myogenic activity, and hence the basal tone, is certainly not equal in all types of small vessels. The smooth muscles of the cutaneous arteriovenous anastomoses resemble the intrinsic eye muscles, both in that they are normally quite dominated by the central nervous system via the autonomic nerves and that these specialized smooth muscles show very little myogenic activity and consequently little basal vascular tone.

In 1902, Bayliss offered a hypothesis suggesting that the distention offered by the blood pressure may act as mechanical stimulus on vascular smooth muscles. For decades this interesting idea has been almost forgotten, and for the first time in recent years it has been possible to show that this is a factor to consider, though its influence is far from dominant. It has been difficult to understand exactly how such a mechanism operates, but now a reasonable explanation may be offered. It is known from studies of nerve-free intestinal smooth muscle strips, that distention has a facilitatory influence on the rhythmic, inherent activity, increasing the rate of contractions. This may also happen in those parts of the vascular bed where the smooth muscles exhibit myogenic activity. In fact, it has been observed in the vessels of the bat's wings, where the rate of rhythmic "vasomotion" has been observed to increase as a response to steady distention of the vessels. This should mean that the time fraction occupied by the constriction phase increases on the expense of relaxation, and the integrated result of this in a vascular bed is a somewhat increased tone within those sections where myogenic activity occurs. Also, it is then understood why vessels like the cutaneous arteriovenous shunts do not increase their tone as a response to distention; these centrally dominated vessels hardly show any myogenic activity that could be facilitated.

The origin of the "basic activity" of the vascular smooth muscle cells has been discussed, now we will concentrate our interest on the powerful, superimposed influence of the vasoconstrictor fibers. Vasoconstrictor fiber distribution shows a considerable differentiation, with a tendency of an inverse relationship between the extent of basal tone and constrictor fiber supply. To mention the extremes, the heat-loss regulating cutaneous arteriovenous shunts, which serve no local needs but the organism as a whole, are supplied with an abundance of constrictor fibers but have, as mentioned, hardly any basal tone. In contrast, vessels subserving the metabolic needs of vitally important tissues, like the brain or the myocardium, have only few constrictor fibers but nevertheless a considerable "blood flow reserve" in the form of their locally controlled basal tone. Between these extremes the other vascular circuits are found. In generalized sympathetic discharges, as found with hemorrhage, this distribution will have the consequence that the reduced
cardiac output will primarily be delivered to the vital, important tissues.

It should be remembered that effector cells can exhibit various degrees of sensitivity to the constrictor mediator in different vascular areas. It has already been mentioned, for instance, that a given norepinephrine concentration has a stronger effect on the cutaneous arteriovenous shunts than on the vessels of the skeletal muscles.

It is also of importance that the vascular smooth muscles appear to vary in their sensitivity to locally produced vasodilator influences. This factor also determines the vascular response to constrictor fiber activation, as the reduced flow leads to an accumulation of vasodilator factors which counteract the effect of the constrictor fiber mediator. Differences in smooth muscle sensitivity can be strikingly illustrated if one compares muscle and cutaneous vessels. Lastly, the wall-to-lumen ratio of the vessels influences the hemodynamic result of a given sympathetic vasoconstrictor fiber activation.

What then is the influence of the main physiologic variable, the extent of vasoconstrictor fiber recruitment and its discharge range? It is obvious both from the classical neurophysiologic studies of Bronk et al. some 20 years ago and from other types of experimental approaches,6,7 that the physiologic discharge rate of visceromotor fibers hardly ever exceeds about 10 impulses per second, even under extreme excitation of the centers. Higher frequencies are, in fact, hardly needed because the almost maximally obtainable effector response to nerve stimulation is then reached. "Normal" vasoconstrictor tone appears to be maintained by a joint activity of most fibers to a given vascular area, firing at rates of only 1 or 2 impulses per second. If one compares the visceromotor neuroeffectors with the somatomotor ones, there is a fairly good 1-to-10 relationship in fiber diameters, refractory period, physiologic discharge range, and frequency response characteristics of the respective effector cells.

As mentioned earlier, the hormonal sympathetic link has, in most areas, fairly insignificant excitatory effects on the cardiovascular system when compared with the direct vasoconstrictor innervation. The situation is quite different for the inhibitory influences, i.e., the vasodilation induced by blood-borne epinephrine in tissues like the myocardium and the skeletal muscles. Even the minute blood concentrations obtained at low-frequency fiber discharge, can elicit rather powerful vasodilatations, and this reaction is normally the most important cardiovascular effect of the hormonal link on generalized sympathetic excitation, i.e., it may contribute significantly to divert the cardiac output to the muscles and heart.14,21 That the hormonal link is of relatively insignificant importance in many respects is hardly surprising; its diffuse and relatively slow action would otherwise make rapid and differentiated cardiovascular adjustments impossible; such adjustments must be executed by a dominating, direct nervous link. In this area some very important questions concerning the nervous control of the vessels are raised: 1. Do similar differentiations in fiber distribution, etc., occur between the different consecutive sections of a vascular circuit? 2. Are there also strictly regional differences in discharge rate, and, if so, how extensive? Earlier the sympathetic nervous system was mainly looked upon as a sort of mass activity system and, in some circumstances it is; but this does not exclude the possibility of differentiated reaction patterns. To deal with this aspect it is also advisable to divide the effector system, i.e., the vascular bed, according to its functional specialization. In the first line one can distinguish between the various "parallel-coupled" circuits, e.g., coronary, cerebral, renal, muscular vessels. As already indicated, they often show considerable differences in fiber distribution, effector sensitivity, etc. Further, any of these parallel-coupled circuits can be divided in functionally defined "series-coupled" sections: (1) "Windkessel" vessels, (2) resistance vessels with a precapillary and a postcapillary section, (3) precapillary sphincters, which determine the number of capillaries, and hence the capillary surface, open for perfusion at
any given moment, (4) shunt vessels and, (5) capacitance vessels. All these sections, controlled by smooth muscle cells, are responsible for well-coordinated but essentially separate control functions, all of which, directly or indirectly, cooperate to control the flow through the most important section of all, the true capillaries. Across the walls of these "exchange vessels" the tissues come in close contact with the mobile fraction of the stable environment. Quite a bit is known about the resistance vessels, much about the capillaries, and some about the shunts, at least the ones in the skin. Relatively little and, in some respects, nothing is known about the range of control of the other sections and their integration with the rest of the circulation. This is mainly because they are far more difficult to study separately with more exact methods. These vascular sections are, however, functionally just as important as the better-studied ones. Changes in tone of the capacitance sections, for instance, will profoundly affect the venous return to the heart and hence the cardiac output. Several attempts have recently been made to develop methods allowing more detailed analyses of the integrated control of capacitance vessels in relation to resistance vessels and heart function. In our laboratory a method has been used, which is somewhat related to the one utilized by Pappenheimer et al. in their classical capillary studies. Our method makes it possible to follow continuously and separately the range of nervous and hormonal control of the precapillary and postcapillary resistance vessels, the capacitance vessels, and to some extent the precapillary sphincters and the cutaneous shunts. The results illustrate that the vasoconstrictor control of the capacitance vessels in the cat's hindbody in some respects is even more powerful than that of the resistance vessels. The hyperbolic curve, relating stimulation frequency to effector response, for the capacitance vessels is displaced to the left of that of the resistance vessels, i.e., at a slight generalized increase of constrictor fiber discharge the "intravascular fluid mobilization" is relatively more pronounced than the increase of flow resistance. The constrictor fiber influence on the 2 sections of the resistance vessels is, generally, more intense on the precapillary section than the postcapillary section, which implies that mean capillary pressure decreases on sympathetic stimulation even if arterial inflow and venous outflow pressures stay the same. This leads to a shift in the Starling equilibrium across the capillary walls, so that tissue fluid passes into the blood stream. The constrictor fiber control of the resistance vessels therefore implies possibilities of an "extravascular fluid mobilization" to the vascular compartments. Lastly, the sphincter sections are to some extent influenced by constrictor fibers, though not so markedly. There occurs an unquestionable decrease in capillary surface area available for perfusion, presumably because constrictor fiber activation causes a fraction of the precapillary sphincters to obstruct flow through their respective capillaries.

Results indicate that the sympathetic vasoconstrictor fibers to skeletal muscles act almost only on the resistance vessels. Epinephrine, which increases blood flow to the muscles, generally also decreases the blood volume within the muscles, i.e., while it inhibits tone in at least some section of the resistance vessels, it excites the smooth muscles of the capacitance vessels. Further, although norepinephrine strongly contracts both resistance and capacitance vessels, angiotensin has a profound action only on resistance vessels. All these data illustrate differentiations between the different "series-coupled" vascular sections concerning vasoactive fiber distribution and effector sensitivity to transmitters as well as other vasoactive substances.

We then come to the second question: Can, by way of higher centers or cardiovascular receptors, the neuron pools controlling the various parallel, and the series-coupled vessels be more or less separately activated? If so, the nervous control of the vascular bed is indeed far from a diffuse network fitted only for mass activation patterns, but a highly specialized system suited for considerable degrees of differentiation. There is some evi-

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dence in the literature, that such differences do occur between the various parallel circuits though much remains to be done; e.g., the constrictor fiber discharge to the renal or the cutaneous vessels is often not the same as that to other vascular circuits. So far, the series-coupled sections have been inadequately studied with suitable methods to allow any definite statements. However, experiments are going on with the mentioned method, in which the vasomotor fiber connections to the studied region are left entirely intact. Under such circumstances the normal discharge patterns, induced from cardiovascular receptors or higher vasomotor centers, will affect the different consecutive vascular sections of the cat’s hindbody. Though they are undoubtedly fairly equally affected in many reaction patterns, some preliminary observations suggest that striking differentiations in the discharge patterns may also occur under some circumstances. It should be admitted here that the more detailed functional analysis of the autonomic nervous system has been badly neglected, when compared with the somatomotor system. It may ultimately prove to be just as differentiated in its neuroeffector control. Even if it should be found that great differences in regional vasoconstrictor fiber discharge do not occur, it should be stressed that the responses of the effector cells in different vascular sections may nevertheless be strikingly different, simply because of differences also in fiber distribution, effector sensitivity, etc.

A few words should be said about the higher centers controlling the vasoconstrictor fibers. It is well known that the medullary vasomotor center (VMC) is a very capable reflex center, responsible for the tonic control of blood pressure. It is, however, normally continuously modified by the activity of diencephalic and cortical autonomic centers. No details about their organizations will be given here, for which the reader is referred to other review articles, but a few principles should be mentioned. For decades the higher centers of cardiovascular control were more or less neglected, and many investigators as-

sumed that neurogenic circulatory adaptations as in muscular work, were predominantly started in the periphery by way of the cardiovascular proprioceptors and VMC, rather than from the cortex-diencephalon. It might be, however, that the VMC is only one part of the system, a sort of autonomic equivalent to the somatomotor “antigravity center,” and that the higher autonomic centers have numerous direct connections with their “final common path,” the preganglionic cells of the spinal medulla. It becomes more and more clear, and it should have been obvious long ago, that the higher centers generally act as the initiators of cardiovascular adjustments that accompany changes in alertness and the onset of muscular work. The autonomic activation patterns probably run parallel with the somatomotor ones, thus “anticipating” the cardiovascular shifts needed to suit the change in activity. In all probability, however, this central direction of the cardiovascular system is not too exactly balanced, but becomes so when it is automatically adjusted by the cardiovascular receptors via VMC, so that the ultimate pattern results in small changes in pressure and is well regulated to the new level of muscle activity. We may here draw a parallel to the respiratory control, in which a similar interplay between central direction and reflex medullary fine-adjustment appears to take place. Concerning central cardiovascular control, however, our knowledge is still meager indeed but it is a fascinating field of research. Mention only is needed of the hypothalamic temperature control of cutaneous blood flow, the cardiovascular shifts taking place in emotional fainting, anger, fear, and muscular work to indicate the importance and interest it deserves. Its clinical implications are obvious; one need only mention so-called psychosomatic disturbances.

After this short survey of the factors that establish vascular tone a few words should be spent on the factors that inhibit vascular tone, the so-called vasodilator metabolites, released from any active tissue. Whatever they are they constitute a mechanism by which tissues can claim more blood flow whenever needed.
SYMPOSIUM—CARDIOVASCULAR REGULATION

It is evident that the previously mentioned vasodilator fibers can, and do sometimes, contribute to increase the blood flow to activated tissues, but they are in no way indispensable; the local chemical factors are the important ones. Exactly what these factors are is still not clear, though soon 100 years of intense efforts will have been made to solve this problem. The reason why no one as yet identified the factor, responsible for the local dilatation, may simply be that there is not one but many contributory factors. If so, elimination of one factor does not change the dilatation much, though it normally is of importance. We do know that several factors, normally released, have a vasodilator influence. First the basic shifts in internal environment, such as decrease in oxygen tension, increase of carbon dioxide tension, or lowering of pH, should be mentioned; they all tend to relax vascular smooth muscle. It is reasonable to believe that they do so by a direct influence on the muscle cells and not only via a release of other dilator agents. This does not exclude that such factors cooperate. Of known tissue metabolites, carbon dioxide, lactic acid, and adenosine compounds appear to be the only ones that can be expected to cause any significant vasodilatation. It should further be remembered that on tissue activation a slight increase in extracellular potassium concentration takes place and such a chemical shift also has a vasodilator influence. The adenosine compounds, being released at the very start of cell excitation, have a profound vasodilator action, but no one knows whether they really diffuse out of the cells in significant amounts, which is the prerequisite to reach the blood vessels. Once again it has been suggested that also quite specific vasodilator agents should be produced. Thus histamine and acetylcholine have here been discussed, but there is nothing at present to indicate that they should play any significant role in this respect. The only known factor that can be called a specific vasodilator agent is the previously mentioned bradykinin, released from activated gland cells. It appears to be released only from this type of tissue, however, and may here play the role to cover the double demand of blood flow, both for metabolism and for production of secretion. On the whole, it may seem surprising that we know so little about this fundamental question, but the fact is that it is extremely difficult to attack experimentally.

The question now arises: is the blood flow per se regulated? In a way it is, in a way it is not, it depends very much on what is meant exactly by the word "regulated." The tissues have their local mechanisms capable of increasing their blood supply in a good balance to what is their actual nutritional demand; but the organism as a whole cannot always allow any tissue to make free use of its "blood flow reserve." There is an upper limit of cardiac output and often stress situations have seriously restricted the pump capacity. Under such circumstances the most important and most sensitive tissues, the heart and the brain, must be supplied first. Therefore, superimposed upon the local dilator control we have the restricting influence of the vasoconstrictor fiber system, so organized in its distribution, discharge, etc. that it has the power to give the biggest rations of the decreasing cardiac output to those tissues that need it most. It does so by maintaining as long as possible, a suitable perfusion pressure to these areas, which, due to the characteristics of constrictor fiber distribution are not exposed to flow restriction. Therefore, in discussing regulation of blood flow, one has to judge the steady balance between the local demands and the superimposed, restricting system, acting as the maintainer of a suitable perfusion pressure for the most important tissues. No doubt, there are here many important things that we still know too little about, and it cannot be said that we at present know exactly how the blood to the tissues is controlled or regulated.

Summario in Interlingua

Il es generalmente reconoschite que alterationes del tono in le musculatura lisie del vasos es exquisitemente importante in determinar alterationes del fluxo de sanguine. Es etiam generalmente acceptate como un facto que inter le factores que influe super le tono

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vasomuscular le factor nerve es le plus importante, sed il remane un question controverses quant e qual mechanismes specifie es interessate in iste relationes.

Le presente articolo summarisa le conception classie del influentias que determina le tono vascular, confrontante lo con le opiniones currente con attention special prestate al relation inter le mechanisme nervose e altere significative mechanismes. Es discute separatele le factores excitatori, que es primarimente nerve, e le factores inhibitori, inter le quales effectes hormonal pare esser de plus grande importanta.

In conclusion le autor subleva le question de si le studio del factores que determina le tono vasomuscular permette le conclusion que il se tracta hic de un sistema regulatori (per contrasto con mechanismos simplemente determinatorii). Le autor summarissu su analysi de iste question in le assertion que multe importante factos in iste campo de investigation remane inadeguamente clar, de maniera que il non es possibile a iste tempore dicer con precision como le provision de sanguine al tissus es determinate o regulate.

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