SPECIAL ARTICLE

Role of the Veins in the Circulation

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PUMPING, resistance, and capacitance elements constitute the essential components of the cardiovascular system. Although no part of this system can claim a single function, anatomic studies make it obvious that the postcapillary vessels contain the largest proportion of the total blood volume and constitute the reservoir of the circulation. This review will emphasize some of the ways in which capacitative changes in this reservoir, largely residing in the veins, are integrated with the pumping and resistance elements of the circulation. Although statements are frequently made that 65 to 75% of the total blood volume is contained in this reservoir, such figures are anatomic guesses, and understandably no one has devised a method for accurately determining this volume in life.

The role of the postcapillary vessels of the systemic circulation differs markedly from that of the precapillary vessels. The latter constitute a system of conceptually parallel tubes which by alterations in their caliber dictate the distribution of the left ventricular output. This caliber is controlled predominantly by local chemical changes in the organs and tissues of the body, thus providing for distribution of blood in accordance with local metabolic needs. Reflexes operating via the sympathetic nerves integrate the local changes with the total changes in systemic vascular resistance.

By contrast, the postcapillary vessels of the various systemic vascular beds appear to be unaffected by local regulatory mechanisms and act in uniformity as part of the total reservoir system. This system, because of its visco-elastic properties, may markedly change its volume passively with small changes in transmural pressure; and, by virtue of the smooth muscle in its walls, it can actively change its volume, and concomitantly the intraluminal pressure, through a centrally integrated neurogenic mechanism. Although in the past certain parts of this capacitance system, such as the spleen, liver, and skin, have been regarded as specific blood depots, these are components of the total system and do not function independently of it; little would be gained by releasing blood from one portion of the venous system merely to sequester it in another.

The reflex changes in wall tension on the efferent side are mediated by sympathetic adrenergic nerves. Studies on the capacity vessels of the limb of the dog have given an indication of the sensitivity of this system. Electrical stimulation of the lumbar sympathetic chain once every 5 seconds has been sufficient to cause an increase in wall tension. Further increases are graded to the frequency of stimulation; a maximum is reached at about 10 impulses/second.¹

Knowledge of the behavior of this capacitance system in humans is limited largely to studies made on the limbs, wherein it is perhaps more readily appreciated that the veins constitute the main part of the system. Two methods have been used. In the first, the pressure is measured in a small segment of vein free from tributaries which is temporarily isolated from the rest of the circulation,² or the pressure is measured in a large vein of a limb distal to a pneumatic cuff inflated sufficiently to cause complete arrest of the

¹From the Mayo Clinic and Mayo Foundation, Rochester, Minnesota.
THE VEINS circulation (fig. 1). In such circumstances the vein or veins contain a constant volume of blood, and the changes in pressure are proportional to reflexly mediated changes in tension of the smooth muscle of the vein wall. In the second method, the changes in volume in a limb are determined when the vessels, mainly the veins, are subjected to different distending pressure. Since in this latter method blood flow through the limb continues, it gives information about the volume of blood which can be expelled or collected in the part when local, humoral, or nervous stimuli are applied (fig. 2); occasionally, difficulties in interpretation arise due to uncertainties concerning variations in the basal volume of blood in the veins and in the contribution of vessels other than the capacity vessels to the observed volume changes.

Before enumerating the conclusions that can be drawn from these studies, it is convenient to define the term vascular “tone.” For purposes of the present discussion, the original definition will be used. To earlier workers, tone as applied to the blood vessels meant the degree of activity of the smooth muscle fibers of the vessel wall. A change in tone occurred when this degree of activity was altered by local, humoral, or nervous factors. Today, vascular tone or stiffness is defined as the factors which determine the vessel radius at a given distending pressure. These include, in addition to the activity of the smooth muscle, such factors as the connective tissue and the water and electrolyte content of the vessel wall. However, since dynamic changes in vessel caliber occur as a consequence of alteration in activity of the vascular smooth muscle, it is useful to use the

Figure 1

Effect of voluntary hyperventilation on venous tone. Two minutes before these observations were made circulation to right foot was arrested by a pneumatic cuff around ankle inflated to 300 mm Hg. Note increase in venous pressure in a foot vein due to reflex increase in tension of vein wall as a consequence of hyperventilation. This subject also shows rhythmic fluctuations in venous pressure; it is uncommon to see these in other veins in the limbs.
exercising limbs. The increase, which can be detected during leg exercise in the supine subject at a work intensity corresponding to an oxygen uptake of about 950 ml STPD/minute, is graded to the severity of the work.9-11 This stiffening of the venous system in combination with the muscle and the abdominothoracic pump aids venous return. At the same time there is an active increase in tension in the smooth muscle of the resistance vessels of vascular beds of nonexercising parts so that the increase in left ventricular output is distributed mainly to the active muscles.12-14 These responses are abolished by sympathectomy and by drugs which interfere with the release of, or cause depletion of, the sympathetic neurotransmitter.15 As a consequence, there is a decrease rather than an increase in systemic arterial blood pressure in subjects who perform muscular exercise after receiving guanethidine.16 Local heating of the limbs also reduces or abolishes the response, suggesting that it may not be as effective in a hot environment, unless adaptations occur.17 The receptors and afferent pathways concerned in these reflex adaptations are unknown. Patients with congestive heart failure have an increased tone of the forearm veins at rest, which is postulated to result from increased activity of sympathetic nerves; the tone increases further with leg exercise of a degree which does not cause vasoconstriction in patients who have compensated heart disease.18, 19 The intravenous administration of ouabain may diminish the vasoconstriction in patients with congestive failure but may cause vasoconstriction in normal subjects.19 To explain this, it is suggested that the improvement in cardiac function due to ouabain diminishes the reflex vasoconstriction so that the resultant decrease in tone exceeds the increase due to the direct effect of ouabain on the vessels.

During an emotional stress, some of the circulatory changes correspond to those seen with exercise. There is constriction of resistance vessels in the viscera and dilatation of the resistance vessels in muscle,20 along with reflex constriction of the capacity vessels in the

**Figure 2**

Typical relationship between increase in forearm volume and pressure in a large forearm vein at rest (♦) and during supine leg exercise (○). Forearm blood flow was similar in both circumstances. (Reproduced from J Appl Physiol 20:1, 1965, with permission of the publisher.)

word “tone” in its earlier context to describe these changes.

Under comfortable environmental conditions, there is little or no activity in the sympathetic nerve fibers to the veins. The tone of the smooth muscle in their walls is at a minimum, and the volume of and pressure in the capacity system is dictated by the visco-elastic properties of the vessel wall. In contrast, the smooth muscle of the resistance vessels (small arteries and arterioles) has a high degree of tone, because of activity of the sympathetic adrenergic nerves and of local or humoral agents which are still ill-defined. Thus, abolition of adrenergic nerve activity, infusions of vasodilator substances into the artery supplying the limb, local exercise of the part, or application of heat can cause a marked dilatation of the resistance vessels, but does not change the amount of blood that can be held in the capacity vessels at any congesting pressure.6-8

Muscular exercise causes, in normal subjects, a sustained reflex increase in tone of the venous walls in both exercising and non-exercising limbs. The increase, which can be detected during leg exercise in the supine subject at a work intensity corresponding to an oxygen uptake of about 950 ml STPD/minute, is graded to the severity of the work.9-11 This stiffening of the venous system in combination with the muscle and the abdominothoracic pump aids venous return. At the same time there is an active increase in tension in the smooth muscle of the resistance vessels of vascular beds of nonexercising parts so that the increase in left ventricular output is distributed mainly to the active muscles.12-14 These responses are abolished by sympathectomy and by drugs which interfere with the release of, or cause depletion of, the sympathetic neurotransmitter.15 As a consequence, there is a decrease rather than an increase in systemic arterial blood pressure in subjects who perform muscular exercise after receiving guanethidine.16 Local heating of the limbs also reduces or abolishes the response, suggesting that it may not be as effective in a hot environment, unless adaptations occur.17 The receptors and afferent pathways concerned in these reflex adaptations are unknown. Patients with congestive heart failure have an increased tone of the forearm veins at rest, which is postulated to result from increased activity of sympathetic nerves; the tone increases further with leg exercise of a degree which does not cause vasoconstriction in patients who have compensated heart disease.18, 19 The intravenous administration of ouabain may diminish the vasoconstriction in patients with congestive failure but may cause vasoconstriction in normal subjects.19 To explain this, it is suggested that the improvement in cardiac function due to ouabain diminishes the reflex vasoconstriction so that the resultant decrease in tone exceeds the increase due to the direct effect of ouabain on the vessels.

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Circulation, Volume XXXIII, March 1966
limbs.\textsuperscript{2} A deep breath or a period of hyper-ventilation\textsuperscript{2, 4, 9, 21} also causes constriction of the capacity vessels via sympathetic adrenergic fibers, and it is of interest that a person feeling faint may engage in sighing respiration. Other sensory stimuli, such as placing the feet in cold water,\textsuperscript{4} can cause marked reflex constriction of the capacity system.

Surprisingly—since it is contrary to what is often taught—when a normal subject is tilted into the upright position, or a change in posture is simulated by transferring a considerable volume of blood to the legs of a horizontal subject by applying subatmospheric pressure to the parts of the body below the iliac crests,\textsuperscript{22} there is no sustained increase in tone in the capacity vessels. Transient increases may occur at the moment of tilting, but these are due not to the shifts of blood but to an involuntary deep breath or to psychic influences associated with the tilting or the application of the suction. It is the resistance vessels, by their maintained reflex constriction which controls the rate of accumulation of blood in the dependent parts, that play the predominant role in the maintenance of systemic arterial pressure in the upright position.\textsuperscript{23} We have observed a patient with idiopathic orthostatic hypotension whose limb veins constricted normally to a reflex stimulus such as a deep breath but who showed the typical fall in systemic arterial pressure on standing, due to failure of the resistance vessels to constrict.\textsuperscript{23} The receptors concerned in this reflex constriction of the resistance vessels have not been established. Stimuli which decrease intrathoracic blood volume, such as tilting head-up and positive-pressure breathing, cause reflex constriction; and those which increase intrathoracic blood volume, such as negative-pressure breathing and tilting head-down, cause reflex dilatation of resistance vessels. These changes in volume could activate receptors in the low-pressure vascular compartments in the chest with resultant selective changes in activity of the sympathetic adrenergic fibers to the resistance vessels,\textsuperscript{24} with or without minimal alterations in activity to the capacity vessels.\textsuperscript{25}

The high-pressure baroreceptors may also be involved in some of these reflex responses to head-up tilting or to radial acceleration. Experiments in dogs and some in man have demonstrated that the reflex changes in caliber of the systemic resistance vessels caused by changes in carotid sinus pressure are accompanied by minor or no changes in tone in the capacity vessels.\textsuperscript{26, 27} In dogs, decreases of 150 mm Hg in sinus pressure caused responses in the resistance vessels of the limb equivalent to sympathetic chain stimulation at 6 to 7 impulses/second—a rate near to the top of the physiological range\textsuperscript{28} and an increase in venous tone equivalent to less than 0.5 impulse/second—a rate near the threshold level at the lower end of the stimulus response curve.\textsuperscript{1} The widespread belief that the veins play an important role in the responses associated with the carotid sinus reflex is based on the concept that a widespread constriction of systemic veins, by causing an increase in cardiac output, contributes to the increase in systemic arterial pressure which results from a decrease in carotid sinus pressure. However, recent studies with a variety of independent methods have shown that there is no change in cardiac output of consequence, that there is no shift of blood from the systemic to the intrathoracic vascular bed, such as might be caused by widespread constriction of systemic veins, and that the increase in systemic pressure is due to the reflex constriction of the resistance vessels.\textsuperscript{26} Since the carotid sinus mechanism has relatively little effect on the capacity system, there is during exercise no reflex venodilatation to oppose the reflex venoconstriction as the systemic arterial pressure rises in proportion to the severity of the exercise.\textsuperscript{29}

As mentioned above, changes in distribution of blood by gravitational or other forces cause selective changes in sympathetic activity to resistance vessels as do changes in carotid sinus pressure. Occasionally, when dogs are examined under a variety of stimuli, differential alterations in activity of adrenergic nerve fibers can be seen, constriction of capacity vessels occurring simultaneously with
dilatation of resistance vessels, and vice versa. Thus the vasomotor centers are able to alter selectively the nervous activity of the adrenergic fibers to the veins and resistance vessels, at least to those in the limbs.\textsuperscript{30}

Armchair consideration of the integration of the control of the systemic vascular reservoir with the total circulation would suggest that a reflex increase in its wall tension would be most advantageous when there is an increase in cardiac output and a decrease in the total systemic vascular resistance. Such an increase in wall tension would reduce the time constant of the capacitative venous system, maintain or increase the filling pressure of the right ventricle, provide the blood necessary to fill the expanded capillary bed of the lungs and of the systemic precapillary and capillary vessels, and contribute to the filling pressure of the left ventricle. Such evidence as we have in the limbs suggests that the peripheral veins react more strongly than the proximal ones to a reflex stimulus,\textsuperscript{4} and one might speculate that the capacity system as a whole is well equipped to move blood centrally. The fact that muscular exercise, hyperventilation, strong emotional stimuli, and cold showers,\textsuperscript{31, 32} all of which increase cardiac output with a decrease in systemic vascular resistance, are associated with reflex venoconstriction in the limbs supports this hypothesis. When there is an increased systemic vascular resistance with a decrease in cardiac output, as occurs on the assumption of the passive erect posture, or little change in output, as with carotid sinus hypotension, no shift in blood is required, and the accompanying increase in sympathetic activity to the myocardium enhances its function, without the necessity of increasing the filling pressure of the ventricles.\textsuperscript{33}

The newer pharmacological agents which cause selective block of the so-called alpha and beta adrenergic receptor sites in the vascular system have provided useful tools for the analysis of the effects of sympathomimetic agents on the resistance and the capacity vessels. The intravenous administration of the beta adrenergic receptor stimulator, isoproterenol, causes dilatation of resistance vessels, increased cardiac output, and constriction of systemic capacity vessels.\textsuperscript{34} All of these actions are eliminated by a beta-receptor-blocking agent.\textsuperscript{35} The administration of phenylephrine or norepinephrine, which are alpha-receptor-stimulating agents, causes constriction of both resistance and capacity vessels, and these actions are blocked by an alpha-receptor-blocking agent, phenoxybenzamine. Thus, while stimulation of alpha and beta receptors causes opposite effects on the resistance vessels, stimulation of either causes constriction of the smooth muscle of the capacity vessels.\textsuperscript{35} Epinephrine, which stimulated both types of receptors when given intravenously at 10 to 15 \mu g/minute in man, causes a 47, 25, and 15\% increase in cardiac output, stroke volume, and heart rate, respectively.\textsuperscript{36} There is a decrease in total systemic resistance due to dilatation of resistance vessels in muscle, and a decrease in venous distensibility.\textsuperscript{37} Thus as in muscular exercise, so with isoproterenol or epinephrine infusions: the venous constriction is a valuable asset and a logical accompaniment of increased cardiac output and decreased total systemic vascular resistance (table 1).

The systemic vascular reservoir works in conjunction with the pulmonary vascular reservoir. When blood is added to the vascular system of dogs, the lungs and heart increase their volume in proportion to the increase in total blood volume.\textsuperscript{39} When a supine subject stands upright in a relaxed manner, 300 to 800 ml more blood is contained in the legs,\textsuperscript{40} and the volume of blood extending from the right atrium to the root of the aorta decreases by about 20\%.\textsuperscript{41} Mild exercise in this position by the venous pumping action of the legs returns the intrathoracic volume to its supine value,\textsuperscript{41} so that the pulmonary capillary blood volume is increased, and there is increased perfusion of the upper zone of the lungs.\textsuperscript{42} With increasing cardiac output, as exercise up to the maximum possible is performed, there is little further augmentation of the intrathoracic blood volume.\textsuperscript{41} Under steady-state conditions, it probably remains remark-
Table 1

Response of Cardiac Output, Resistance, and Capacity Vessels to Various Stimuli*

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Cardiac output</th>
<th>Resistance</th>
<th>Wall tension of capacity system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
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<tr>
<td>Emotion</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
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<tr>
<td>Cold shower</td>
<td>↑</td>
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<td>↑</td>
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<tr>
<td>Severe anemia</td>
<td>↑</td>
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<tr>
<td>Beriberi</td>
<td>↑</td>
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<tr>
<td>Isoproterenol</td>
<td>↑</td>
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<tr>
<td>Epinephrine</td>
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<tr>
<td>Upright posture</td>
<td>↓</td>
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</tr>
<tr>
<td>Carotid sinus</td>
<td></td>
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<tr>
<td>Hypotension</td>
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<tr>
<td>Carotid sinus</td>
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<tr>
<td>Hypertension</td>
<td>↓</td>
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</tr>
</tbody>
</table>

*Only the direction of the changes is given (↑ increased; ↓ decreased; — no change) with no indication of the magnitude. The resistance is the total systemic vascular resistance—that is, the resistance to outflow from the left ventricle and not that of individual vascular beds. Thus with exercise, emotion, epinephrine, and other stimuli the vasodilatation in the skeletal muscles occurs simultaneously with a constriction of other vascular beds, but the over-all resistance is decreased. The capacity is the volume of the total systemic postcapillary bed; the changes indicated are the alterations in wall tension of the capacity vessels in the limbs to the stimuli listed. These changes, like those of the resistance vessels, are due to active changes in tension in the smooth muscle of the capacity vessels, and the author has made the assumption that these reflect the behavior of the total system. (For references, see text.)

The data in the table suggest that an active increase in tension in the walls of the systemic capacitance venous system accompanies an increased cardiac output and a decreased resistance to outflow from the left ventricle. Conversely, where there is little change or a decrease in cardiac output, and little change or an increase in resistance to outflow, there is no active increase in tension of the capacity system.

Data from Sharpey-Schafer, Brit M J 2: 1569, 1961. The method he used to detect changes in venous tone has been criticized by later workers so that the response of the veins to these conditions has to be confirmed.

ably constant due to the ability of each ventricle to adjust its stroke volume independently via changes in filling pressure. One of the seminars which preceded the 1965 annual meeting of the American Heart Association was on the venous system and its control. This seminar, organized by the Council on Circulation, provided an opportunity to review present knowledge. It served to emphasize that in man our knowledge of the capacity system is confined almost entirely to studies made on the limbs and that the results of these studies are sometimes difficult to interpret, owing to the limitations of available methods. Much has still to be learned of the control of the systemic and pulmonary capacity systems and their integration with the pumping and resistance components of the circulation.

References


After Galen

In the eleventh century, Ibn Sina (Avicenna), who had integrated all Greek and Moslem knowledge in his famous Canon, still adhered strictly to the description of the heart and lungs given by Galen. This was considered sound doctrine until the middle of the thirteenth century, when Ibn Nafis, an Arab physician born in Damascus in 1210, who was also a philologist and a theologian, presented some divergent points of view in his Commentary on the Anatomy of Avicenna’s Canon and rejected Galen’s assumption of interventricular pores.

“The blood (of the right ventricle) passes through the vena arteriosa (= pulmonary artery) to the lung, spreads through its substance, mixes with the air and becomes completely purified; then it passes through the arteria venosa (= pulmonary vein) to reach the left chamber of the heart.”—ANDRÉ COURNAND, M.D. Circulation of the Blood. Edited by Alfred P. Fishman, M.D., and Dickinson W. Richards, M.D. New York, Oxford University Press, 1964, p. 15.
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Circulation. 1966;33:484-491
doi: 10.1161/01.CIR.33.3.484

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/33/3/484.citation

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