

Shear Forces and Blood Vessel Radii in the Cardiovascular System

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ABSTRACT What mathematical or physiological principles govern the radii of blood vessels in the cardiovascular system and by what mechanisms are these principles implemented? This question is studied in the contexts of fluid dynamics and physiology of the cardiovascular system, and a possible answer is examined in the light of empirical data.

INTRODUCTION

The power H required to pump a fluid of viscosity η through a tube of radius r and length l , at a steady rate of flow f and under conditions of fully developed Poiseuille flow, is given by

$$H = 8\eta lf^2/\pi r^4. \quad (1)$$

A well-known implication of this simple formula is the result that almost 94% of this power can be saved by simply doubling the radius of the tube, all else being unchanged. In other words, only 6% of the power is needed to maintain the same flow of the same fluid through a tube of the same length but double the radius. Consider the circulation of blood in the cardiovascular system, using only approximate data to illustrate the point and ignoring the pulsatile nature of the flow and many other complications at this stage so as not to confuse the issue in hand. Taking $\eta = 0.03$ poise for the viscosity of blood, consider a blood vessel segment of length $l = 10$ cm in which the flow $f = 100$ cm³/s. If the vessel radius is 1 cm, the power required to maintain the flow is 7,640 ergs/s or approximately 16 cal/day. If the vessel radius is doubled, all else being unchanged, the power required is only 1 cal/day. And if the vessel radius is halved, the power required is 256 cal/day. For the cardiovascular system as a whole, the pumping power required from the heart can be estimated from another form of Eq. (1), namely

$$H = f\Delta P, \quad (2)$$

where ΔP is the total pressure drop in the systemic and pulmonary circuits and f is the cardiac output. If one takes $\Delta P = 120$ mm Hg and $f = 100$ cm³/s, Eq. (2) gives $H \approx 33$ Cal/day. Now, if all blood vessels in the cardiovascular system were of double their normal radii while still conveying the same flow, the pumping power required from the heart would be approximately 2 Cal/day. If the vessels were of half their normal radii, the pumping power would be 528 Cal/day. If one assumes, rather generously, that the cardiac efficiency is 10%, the correspond-

ing metabolic rates of the heart would be 330 Cal/day for the system with normal radii, 20 Cal/day for the system with double the normal radii, and 5,280 Cal/day for the system with half the normal radii. Expressed in terms of the total metabolic rate of the host organism, which is approximately 2,500 Cal/day for an average man at rest, these metabolic rates of the heart represent approximately 13% of the total if the vascular system has normal radii, only 1% of the total if the system has double the normal radii, and more than 200% of the total if the system has half the normal radii.

These simple considerations leave little doubt that the radii of blood vessels in the cardiovascular system are the outcome of a very careful and deliberate design, and the following question therefore presents itself in an unequivocal manner. What principles govern the radii of blood vessels in the cardiovascular system and by what mechanisms are these principles implemented? This question has many important implications in cardiovascular physiology and cardiovascular disease.

In studies of the heart and heart failure for example, it has long been recognized that the cardiac effort and efficiency and the aortic pressure against which the heart must pump are major factors (Starling and Visscher, 1927; Peters and Visscher, 1936; Visscher, 1937, 1938; Sarnoff et al., 1958; Braunwald, 1958; Katz and Feinberg, 1958). All these factors are strongly affected by the optimality of vascular radii. In the study of aneurysms at arterial junctions it has been suggested that local hemodynamic events may play a major role in the pathogenesis of this lesion (Roach et al., 1972). These events depend critically on the geometry of arterial junctions which, in turn, depends on the relative radii of the vessels involved in each junction. In the vascular beds surrounding localized cancerous tumors it has been observed that the cardiovascular system has the capacity to form new vessels and/or increase the radii of existing vessels on a strictly local and ad hoc basis (Algire and Chalkley, 1945; Warren and Shubik, 1966; Warren, 1968). By what mechanisms are these changes achieved? And can these mechanisms be reversed so as to diminish rather than increase the blood supply to a localized tumor? In the study of atherosclerosis, some theories ascribe a major role in the pathogenesis of this lesion to the shear force between blood and vessel tissue (Fry, 1968, 1969*a, b*, 1973; Caro et al., 1971; Caro, 1973). This shear force τ depends critically on the vessel radius r as can be seen from Poiseuille's formula

$$\tau = 4\eta f / \pi r^3. \quad (3)$$

Thus if an abnormal shear level, high or low, is indeed a pathogenetic mechanism of atherosclerosis, it is important to ask first what is the "normal" shear level in blood vessels. Clearly, this question is coupled with that of the optimum radii of the vessels.

To each of these and other problems in the cardiovascular system there may be an ad hoc solution and, insofar as clinical considerations dictate, one should aim perhaps unswervingly at the discovery of these solutions. But a thorough physiological understanding of these problems requires a thorough understanding of the operation and design aspects of the system which they afflict. The hemodynamic events which are implicated in these problems depend critically on the radii of the blood vessels involved. An inquiry is appropriate, therefore,

into the physiological factors and principles which govern these radii. The present study is devoted to this question.

THE COST OF BLOOD VOLUME CONCEPT

If the length of a blood vessel is kept constant, an obvious effect of a change in its radius is a change in the lumen volume of that vessel. Thus if the radii of all blood vessels in the cardiovascular system were uniformly larger or smaller, the volume of blood contained in the vascular system would be correspondingly larger or smaller. While requiring less pumping power for circulating the blood, therefore, a cardiovascular system with uniformly larger vessel radii would entail a higher metabolic rate for the constant production and maintenance of a larger volume of blood. These considerations led Murray (1926) to the thesis that the radii of blood vessels in the cardiovascular system are the outcome of a compromise between the pumping power on the one hand and what he called "the cost of blood volume" on the other. The quantitative nature of this compromise can be readily derived as follows.

Consider a blood vessel segment of length l and radius r . The pumping power associated with the vessel is given by Eq. (1). In addition to this, an amount of power is needed for maintenance of the blood tissue needed to fill the vessel. Murray (1926) postulated that this maintenance power is proportional to blood volume. For the vessel segment under consideration, therefore, the cost of blood volume is $k\pi r^2 l$ where k is a constant, and the total power requirement H_t associated with the vessel is given by

$$H_t = \frac{8\eta l f^2}{\pi r^4} + k\pi r^2 l. \quad (4)$$

This equation illustrates the antagonism between pumping power and the cost of blood volume which are represented by the first and second terms, respectively. If the radius r increases, the first term decreases and the second term increases, and if r decreases the reverse is true. A compromise is reached when the total power H_t is a minimum, and this occurs when

$$\frac{dH_t}{dr} = 0 \quad \text{and} \quad \frac{d^2H_t}{dr^2} > 0. \quad (5)$$

Applying these conditions to Eq. 4, one readily finds, as was reported by Murray (1926), that the compromise occurs at an optimum value of r , to be denoted by r^* , which is given by

$$r^{*6} = 16\eta f^2 / k\pi^2. \quad (6)$$

The minimum power, to be denoted by H_t^* , is then obtained from Eq. (4) by substituting r^* for r to get

$$H_t^* = \frac{8\eta l f^2}{\pi r^{*4}} + k\pi r^{*2} l,$$

and substituting for k from Eq. (6) to get

$$H_t^* = \frac{24\eta l f^2}{\pi r^{*4}}. \quad (7)$$

Thus at optimum conditions the total power is minimum and is equal to three times the pumping power, and the maintenance power is equal to twice the pumping power.

The most important outcome of the foregoing analysis is the result contained in Eq. (6) which indicates that these optimum conditions occur when the radii of blood vessels are proportional to the cube root of the flow which they convey, i.e.

$$r^* \propto f^{1/3}. \quad (8)$$

This result plays an important role in the study of arterial branching (Zamir, 1976 *a, b*). In a symmetrical arterial bifurcation for example, if r_0 denotes the radius of and f_0 the flow in the parent artery, and if r_1 and f_1 denote the radius and flow for each of the two daughter arteries, then $f_0 = 2f_1$ and Eq. (8) yields

$$r_0^{*3} = 2r_1^{*3}. \quad (9)$$

When one introduces the commonly used area ratio β , which for a symmetrical bifurcation is defined by

$$\beta = 2\pi r_1^2 / \pi r_0^2, \quad (10)$$

it follows from Eq. (9) that at optimum conditions

$$\beta = 2^{1/3} \approx 1.26. \quad (11)$$

This result has been in the literature for many decades but it is often surrounded by an air of mystery. Thompson (1942), for example, describes it as "an approximate result, familiar to students in hydrodynamics" and McDonald (1974) describes it as "the average value. . . that is often quoted". It should be made quite clear that the value 1.26 for β in a symmetrical bifurcation is an implication of the cost of blood volume concept. More specifically, it is based on the optimum result that the radii of blood vessels in the cardiovascular system are proportional to the cube root of the flow that they convey. This relation between flows and radii has not been adequately tested so far.

EMPIRICAL DATA

In vivo measurement of the radius of and the flow in a blood vessel is exceedingly difficult, and the search for empirical data on the relation between flows and radii is therefore a somewhat elusive task. Three major texts on the cardiovascular system (Attinger, 1964; Burton, 1965; McDonald, 1974) present tables from which such data can be derived. Close scrutiny of these tables indicates that they all originate at least in part from earlier data by Green (1950) who presents his data with the following comments: "accurate quantitative data are not available for the capacity of the circulatory system. I have, however, made a rough estimate of the relative capacities of the component parts of the circulatory system based in part on measurement from postmortem examinations upon animals and in part on calculations by Mall from detailed microscopic examinations of the mesenteric vascular bed". The data relate to the entire cardiovascular system of a 13-kg dog and are shown graphically in Fig. 1. Also shown in Fig. 1 is the optimum relation between f and r^* as given by Eq. (6) which for the purpose of direct comparison has been written as

$$f = Kr^{*3}, \tag{12}$$

and hence

$$\log f = \log K + \log (r^{*3}), \tag{13}$$

where

$$K = \frac{\pi}{4} \left(\frac{k}{\eta} \right)^{1/2} \tag{14}$$

On the scales of Fig. 1, Eq. (13) represents a family of straight lines, one line for each value of K as shown.

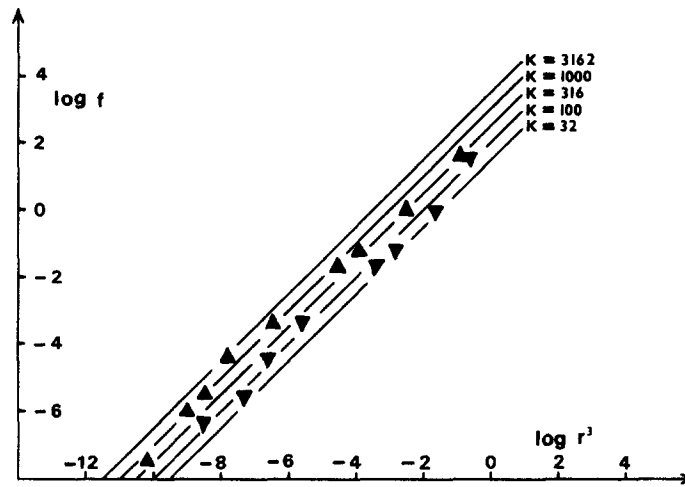


FIGURE 1. Relation between blood flow $f(\text{cm}^3/\text{s})$ and vessel radius $r(\text{cm})$. The solid triangles are based on data by Green (1950) for a 13-kg dog where arteries are represented by ▲ and veins by ▼. The straight lines are based on Eq. (13), namely $\log f = \log K + \log r^3$, with the indicated values of $K(/\text{s})$.

More recently, Iberall (1967) presented a new set of data with the following comments: "For the past thirty years Green's table... has been used as the common quantitative source for data on the arterial tree in mammals. The present paper updates that table by coordinating additional anatomical data from man and dog into a unified model of branching levels". The data relate to the arterial system of a 23-kg dog and are shown graphically in Fig. 2. It should be carefully noted that here too, as in the case of Green's data, many estimates are involved. These estimates are based on work by Mall (1906), Patel et al. (1963), and Suwa et al. (1963).

Suwa et al. (1963) carried out extensive measurements of arterial resin casts and the results were supplemented by estimates of the corresponding blood flows to produce a set of data relating to several organs and major arteries in man. These data are shown graphically in Fig. 3. Suwa et al. explain that in the case of an organ such as the brain, their data refer to a hypothetical arterial trunk which is made up by the union of two internal carotid and two vertebral

arteries, if one assumes a certain power law for arterial branching. Other organs are treated in a similar way.

Wiedeman (1962, 1963) carried out some measurements of the length, diameter, and number of blood vessels in the wing of a living bat. The data relate to one major artery followed by all its branches, capillaries, venules, small veins, and the major collecting vein. Although no flow measurements were made, the flow f at any branching level can be expressed in terms of the flow f_0 in the main artery since $f_0 = nf$ where n is the number of branches at that level. Weideman's

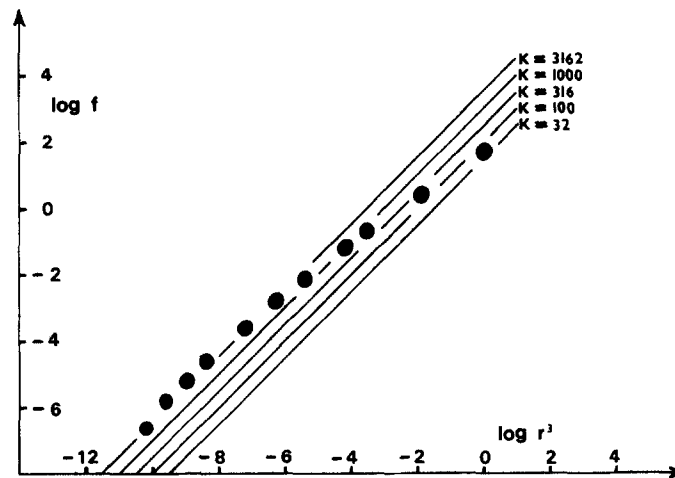


FIGURE 2. Relation between blood flow f (cm^3/s) and vessel radius r (cm). The solid circles are based on data by Iberall (1967) for a 23-kg dog. The straight lines are based on Eq. (13), namely $\log f = \log K + \log r^3$, with the indicated values of K (/s).

results are thus shown in a nondimensional form in Fig. 4, together with a nondimensional form of Eq. (13), namely

$$\log(f/f_0) = \log(K/K_0) + \log(r^3/r_0^3), \quad (15)$$

where suffix 0 refers to the major artery.

Atabek et al. (1975) carried out highly elaborate measurements of the flow field in the left circumflex coronary artery in thoracotomized dogs. In some of the dogs the flow field was measured under normal flow conditions, while in others much higher than normal blood flow rates were induced by intravenous infusion of dipyridamole. The data obtained from the normal cases are shown graphically in Fig. 5.

DISCUSSION AND PRELIMINARY CONCLUSIONS

In Figs. 1-5, empirical data are shown together with the optimum relation $f = Kr^3$ for different values of K . We observe immediately that a fairly wide range of values of K is needed to encompass all the data. On purely mathematical grounds therefore it seems apt to dismiss the theoretical result that f is proportional to r^3 , since proportionality is no longer meaningful when the constant of proportionality is no longer constant. Thus at first sight it appears that the cost

of blood volume principle does not prevail in the cardiovascular system. But we must be cautious, for cardiovascular physiology is not a purely mathematical ground.

First we must consider which parts of the cardiovascular system are likely to be governed by an optimality principle based on the cost of blood volume concept. We recall that while one function of all blood vessels is to convey blood, many vessels perform additional functions. A primary function of the capillaries for example is the exchange of metabolic and waste products and, therefore, capillary radii are likely to be governed by an optimality principle which would

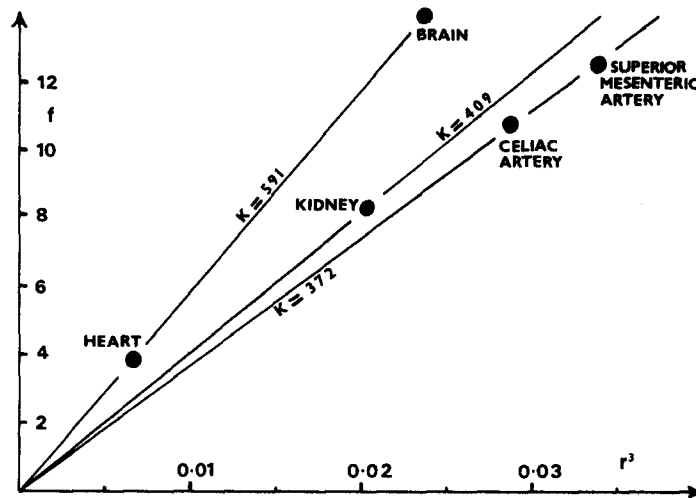


FIGURE 3. Relation between blood flow f (cm^3/s) and vessel radius r (cm). The solid circles are based on data by Suwa et al. (1963) for the indicated organs and blood vessels in man. The straight lines are based on Eq. (12), namely $f = k r^3$, with the indicated values of K ($/\text{s}$).

facilitate this function. A function of the aorta and its main branches is to absorb and modulate the major impact of the cardiac pulse and, therefore, the volume and radii of these large vessels are likely to be particularly suited to this function. In the venous system, the pumping power is of such small significance that it may not play a major role in determining the vessel radii. Part of the cardiovascular system in which the compromise between pumping power and the cost of blood volume may play a major role is perhaps the arterial network between but not including the capillaries and the main arteries. In general it must be remembered that the cardiovascular system is not uniform in function or mode of operation and, therefore, it is unlikely to be uniform in its design aspects. An optimality principle must be matched to the peculiar function and mode of operation of that part of the system in which it is purported to apply. An optimality principle based on the cost of blood volume concept therefore may prevail very strongly in the case of blood vessels whose main function is to convey blood and rather weakly in the case of vessels with other functions. Such variations would manifest themselves quantitatively as different values of K in

different parts of the system, perhaps like the range of values observed in Figs. 1-5.

A more direct test of the cost of blood volume concept can be made by considering the value of the cost of blood constant k . This constant, as defined by Eq. (4), represents the power assumed to be needed for the constant production and maintenance of a unit volume of blood tissue. Under optimum conditions, k is related to the optimum vessel radius r^* by Eq. (6) which gives

$$k = 16\eta f^2 / \pi^2 r^{*6}. \quad (16)$$

Now by combining Eq. (1) and (2) we obtain

$$\Delta P = 8\eta l f / \pi r^4, \quad (17)$$

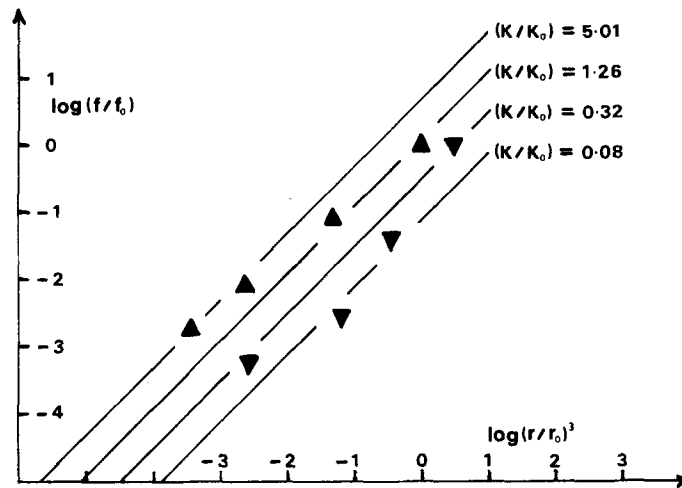


FIGURE 4. Relation between blood flow f and vessel radius r nondimensionalized in terms of the flow f_0 and the radius r_0 of the parent artery. The solid triangles are based on data by Wiedeman (1963) for blood vessels in a bat's wing, where arteries are represented by \blacktriangle and veins by \blacktriangledown . The straight lines are based on Eq. (15), namely $\log(f/f_0) = \log(K/K_0) + \log(r^3/r_0^3)$, with the indicated values of (K/K_0) .

which is a basic Poiseuille flow equation with the following interpretation. With a fixed flow in a blood vessel of a fixed length l , if the vessel radius r is changed the pressure drop ΔP required to maintain the flow will change correspondingly. In particular, when the radius has the optimum value r^* , the pressure drop will have an optimum value ΔP^* and we thus write Eq. (17) as

$$\Delta P^* = 8\eta l f / \pi r^{*4}. \quad (18)$$

Substituting this into Eq. (16), we get finally

$$k = 2f\Delta P^* / V^*, \quad (19)$$

where $V^* = \pi r^{*2} l$ is the volume of a vessel of length l and radius r^* . Eq. (19) is an expression for the value of k as predicted by the cost of blood volume concept. If we apply it to the entire cardiovascular system in man with the approximate data $f = 100 \text{ cm}^3/\text{s}$, $\Delta P^* = 120 \text{ mm Hg}$ and $V^* = 4,500 \text{ cm}^3$, we get

$$k \approx 7,110 \text{ dynes/cm}^2/\text{s} \approx 0.015 \text{ Cal/day/cm}^3. \quad (20)$$

This is to be compared with the metabolic rate of approximately 0.025 Cal/day/g for an average man at rest. The agreement in orders of magnitude is certainly hard to dismiss.

Consider the value of K now, the constant of proportionality between f and r^{*3} as defined by Eq. (14). Substituting $k = 7,110 \text{ dynes/cm}^2/\text{s}$ and $\eta = 0.03 \text{ poise}$ in that equation, we find

$$K \approx 382/\text{s}. \quad (21)$$

When we refer to Figs. 1, 2, 3, and 5, this value of K represents a straight line which is well within and fairly central to the empirical data. In this comparison

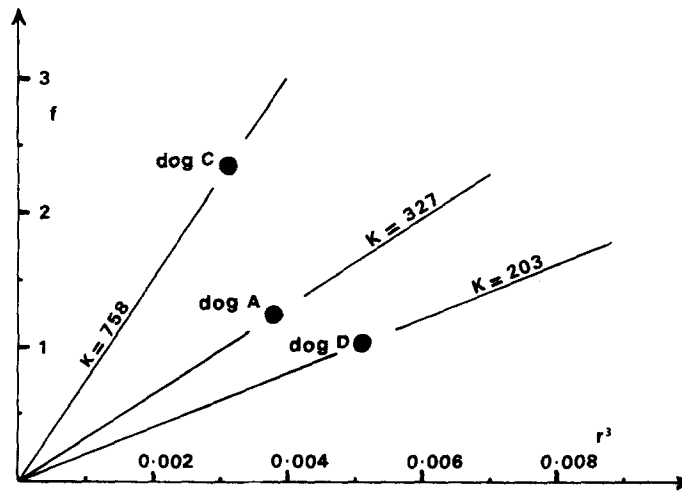


FIGURE 5. Relation between blood flow $f(\text{cm}^3/\text{s})$ and vessel radius $r(\text{cm})$. The solid circles are based on data by Atabek et al. (1975) for the left circumflex coronary artery in dogs. The straight lines are based on Eq. (12), namely $f = Kr^3$, with the indicated values of $K(/\text{s})$.

we must recall that the optimality principle on which this value of K is based is not expected to prevail uniformly throughout the vascular network. Also, this value of K relates to the entire cardiovascular system in man while the data in Figs. 1-5 relate to various parts of the system in three different species.

With all these considerations in mind, it may be safely concluded that the empirical evidence before us is at least not opposed to the theoretical result that the radii of blood vessels in the cardiovascular system are proportional to the cube root of the flow that they convey. It should also be mentioned at the same time, perhaps, that the wide spread of data points may not rule out other possibilities such as a nonlinear relation between f and r^{*3} or a linear relation between f and other powers of r^* . Such alternatives are not being pursued in this study, however, since it is believed that they must first be justified on physiological grounds.

THE CONSTANT SHEAR THEORY

An optimality principle for the radii of blood vessels in the cardiovascular system must be subjected not only to comparison with empirical data but also to the crucial question of the mechanism by which the principle would be implemented. For example, the cost of blood volume concept is well supported by Murray's (1926) physiological arguments and by the value of the cost of blood volume constant k which it predicts in Eq. 20. However, the concept by itself offers no feasible mechanism whereby the radii of individual blood vessels would be controlled by the volume of blood in the entire system.

When supplemented by the optimality principle of minimum power defined by Eq. (4) and (5), however, the cost of blood volume concept moves a step closer to answering the question of mechanism. The compromise between pumping power and blood volume suggests that blood vessel radii are governed by the flow that the vessels convey rather than by the volume of blood in the entire system. Again, this result is well supported by the general observations that a parent blood vessel always carries more flow and has a larger radius than each of its daughter vessels. Thus the question now is how the radii of blood vessels are controlled by the amount of flow which these vessels are designed to convey? An answer to this question is offered by the more specific result that the optimum radii of blood vessels are proportional to the cube root of the flow which they convey. Referring to Eq. (3) for the shear force τ between blood and vessel tissue in Poiseuille flow, we observe immediately that if r is proportional to the cube root of f then the shear force τ becomes a constant.

If pursued to its ultimate conclusion, therefore, the compromise between pumping power and blood volume leads to the theory that blood vessel radii in the cardiovascular system are proportional to the cube root of the flow which they convey and that this principle is implemented by maintaining a constant shear force between the blood and vessel tissue.

While it offers answers to both parts of the question in hand, this "constant shear theory" clearly faces several difficulties. For example, the shear force τ varies periodically in many vessels where the pulsatile nature of the flow still prevails. It also varies considerably when the amount of blood flow is changed with changing activity in different parts of the body. The shear force is not uniform in regions of complex geometry, such as blood vessel junctions. And finally, the wide range of values of K obtained from empirical data tends to dismiss the theory that τ is constant throughout the system. All these difficulties can be resolved, however, if the constant shear theory is stripped from its simple mathematical form and then recast with the complex realities of physiology. If the shear force between blood and vessel tissue is to be monitored and controlled, the endothelial cells must be chiefly responsible for this function since they are the direct recipients of this force. These cells may be the main instrument for maintaining a constant shear in a blood vessel and hence for giving the vessel its optimum radius. In this role, however, endothelial cells are perhaps not sensitive to small or temporary changes in shear but, rather, to large and/or prolonged changes only. Rather than maintain a strictly constant shear force, therefore, the cells would tend to keep the force within a certain range. And since the properties of these cells are not likely to be uniform, this range of shear

may be different in different parts of the system. Thus the "constant" shear theory can accommodate periodic variations in τ as well as different values of K in different parts of the cardiovascular system.

In its physiological form, therefore, the constant shear theory may be stated as follows. The radii of blood vessels in the cardiovascular system are proportional to the cube root of the flow that they convey, the constant of proportionality being a property of the endothelial cells which may be different in different parts of the system. In places where the main function of the vessels is to convey blood, the value of the constant is determined by a compromise between pumping power and the cost of blood volume. In places where the vessels require relatively larger or smaller radii to perform other functions, the value of the constant is correspondingly different.

The sensitivity of endothelial cells to shear forces is well supported by experimental evidence, most notably that of Fry (1968, 1969*a, b*, 1973) and Flaherty et al. (1972). More recently, Rodbard (1975) compiled and documented a great deal of further evidence for the constant shear theory in general, and for the role of endothelial cells in particular. The clinical implications of these findings, with reference to several cardiovascular lesions, are also discussed at some length in that paper.

CONCLUSIONS

Fluid dynamic considerations based on a simple Poiseuille flow model indicate that in order to achieve a compromise between pumping power and the cost of blood volume, the radii of blood vessels in the cardiovascular system must be proportional to the cube root of the flow which they convey.

Empirical evidence, much of which is highly approximate, indicates a general trend towards this rule in the cardiovascular system but the constant of proportionality between the radius and the cube root of the flow appears to have a wide range of values.

Subject to their obvious limitations, these theoretical and empirical findings can be combined into a constant shear theory in which the shear force acting on endothelial cells is the major mechanism for the control of blood vessel radii in the cardiovascular system.

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