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Control of Cardiac Output by Regional Blood Flow Distribution[1]

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Most data indicate that cardiac output is normally controlled by the systemic circulation rather than by the heart. This manuscript extends that concept by analyzing the systemic circulation with a mathematical model comprised of two dissimilar blood flow channels. The concept and the model are not new and have, in fact, a strong anatomical and historical basis. However, re-examination using a quantitative, computerized analysis scaled to human dimensions is made in the face of new experimental data.

The crux of the model is that two parallel blood flow channels have dissimilar compliances. Regional blood flows distribute total blood volume between the two primary blood storage areas, where the blood is more or less effective in promoting venous return according to its location. Changes in cardiac output can theoretically be achieved solely by changes in arterial resistance, without alteration of venous compliance or resistance; this is the situation that is analyzed in detail.

The performance of the model was correlated with experimental data that describe the hemodynamic responses to thoracic aortic constriction, exercise, circulatory shock following endotoxin administration, and other situations. The correlation indicates that redistribution of blood flow following arterial resistance changes can theoretically have a very strong effect on the level of cardiac output, either in a direct causal role or in an ancillary role in conjunction with other, more dominant control mechanisms.

INTRODUCTION

Understanding the control of cardiac output has been difficult because of the closed, circular nature of the intact circulation. Frequently "cause" cannot be distinguished from "effect." This has necessitated adopting an experimental approach where the circulation is conceptually and surgically divided into two separate halves: one half is the heart–lung compartment and the other is all of the remainder of the circulatory system, the systemic circulation. Investigation of the specific hemodynamic characteristics of these two separate aspects of the circulation has shown that the systemic circulation is much more important than the heart in controlling cardiac output in a wide range of circumstances (Guyton *et al.*, 1973). In these instances the heart can easily transfer all blood returning to it across to the arteries of the systemic circulation; the cardiac output is determined by the flow of blood back to the heart, that is, the venous return. However, the im-

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portance of the function of the heart becomes very obvious in high flow situations, such as strenuous exercise, where increased capability is needed to handle the increased venous return. The importance of cardiac function is also obvious in cases of heart failure. But in situations inside of these two extremes, the systemic circulation plays the most important role in the control of cardiac output.

Venous compliance has a strong effect on venous return; decreases in venous compliance increase venous pressure and augment the flow of blood to the right atrium. But in addition, the resistance of the vasculature between the right atrium and the capacitance vessels is another important determinant of cardiac output. These concepts have been combined to describe venous return at any instant as a function of the right atrial pressure, the resistance to venous return, the wall tension of the capacitance vessels and the blood volume in the vessels. In these analyses the peripheral circulation is frequently described as a single blood flow channel running from the output of the left heart to the input of the right heart. Arterial and venous vessels are thought of as two separate blood storage compartments and these compartments are connected in series with each other and with the remainder of the circulation by conduits of the appropriate resistance. Such compartmentalization is rather severe in a mathematical sense because of the great variety of individual vessels in different tissues throughout the body that must be lumped into a single conceptual compartment.

A more detailed analysis, incorporating the concept of parallel flow channels, is warranted on an anatomical basis. The anatomy of the circulation is basically one of a large number of flow channels running in parallel through individual organs such as the brain and kidneys, where only the right atrium and aorta are common to these pathways. The question that is raised is: Are there any important consequences in the overall control of cardiac output that result from parallel vascular beds?

The importance of parallel vascular beds in controlling cardiac output has an historical basis. Krogh in 1912 analyzed a wide variety of previous hemodynamic experiments in terms of parallel flow channels having dissimilar venous compliances. He saw the liver as a very compliant blood storage organ, and felt that cardiac output would be augmented by translocation of blood from this reservoir to the rest of the systemic circulation. Krogh further investigated this concept by building and testing the hydraulic model of the circulation having two parallel vascular channels, one a compliant splanchnic channel and the other a stiff peripheral channel. He then simulated different hemodynamic situations by adjusting resistance and observing changes in pressure and flow. The most notable result was that an *increase* in the arterial resistance of the splanchnic circulation caused an *increase* in cardiac output. This increase in cardiac output was striking in that venous compliance was not changed and that total peripheral resistance was increased.

Barcroft and Samaan in 1935 extended the previous studies of Burton-Opitz (1921) and showed in dogs that occlusion of the aorta distal to the origin of the left subclavian artery caused an *increase* in cardiac output of approximately 30%. This maneuver also produced a translocation of blood away from the viscera, the area made hypotensive by the aortic occlusion. In contrast, Barcroft in 1931 had shown that occlusion of an artery not perfusing the visceral region (the brachioce-

phalic artery) produced a decreased cardiac output. These studies added credibility to the idea that different regions of the circulation could make different relative contributions to the overall control of cardiac output, and that the special contributions were somehow related to the specific venous compliances of the different tissues. Barcroft and Samaan (1935) investigated this concept by building a hydraulic model similar to the one previously used by Krogh; the performance of the model duplicated their experimental data.

Most recently Permutt and colleagues (Sylvester *et al.*, 1973; Stene *et al.*, 1972; Stene and Bromberger-Barnea, 1971; Caldini *et al.*, 1974; Traystman *et al.*, 1973) have applied this concept to hypoxia, hypercapnia, occlusion of the thoracic aorta, and epinephrine infusion and have concluded that redistribution of blood flow is an important determinant of cardiac output in these circumstances. In the case of epinephrine infusion, they were able to estimate the compliances and resistances in the two different parallel pathways by observing the time constants of blood volume changes in these tissues.

These experiments *in toto* have shown the potential importance of the distribution of blood flow in the control of cardiac output. The purpose of this paper is to examine, from theoretical considerations, the possible *quantitative* importance of this phenomenon. A simple model of the circulation, having two parallel blood flow channels in the systemic circulation will be defined. The model will be scaled to human dimensions using available data and will then be tested by observing the sensitivity of venous return and cardiac output to changes in several parameters. The essence of this model is that the two parallel pathways have different venous compliances and, consequently, the model will show different hemodynamic responses to changes in arterial resistance according to the magnitude of the venous compliance downstream from the particular resistance change.

THE MODEL[2]

The model is a simple representation of the intact circulation as shown schematically in Fig. 1. The upper aspect of the model represents the heart–lung compartment while the lower aspect of the model represents the systemic circulation. The systemic circulation has been divided into two subdivisions. One subdivision is entitled the *viscera* and is meant to represent approximately, but not exclusively, blood flow through the organs of the viscera. This subdivision includes the circulation of the liver, all of the organs draining into the portal vein, and the kidneys. The visceral compartment is distinguished by a relatively large venous compliance. The second subdivision is entitled the *periphery* and represents all of the remaining circulation, particularly blood flow through the skeletal muscles, skeleton, brain, and myocardium. This compartment is distinguished by a relatively small venous compliance.

The model has five blood storage areas: the right heart, the lungs, the left heart, the viscera, and the periphery. Each of these blood storage areas has a compliance (C) in units of ml/mm Hg. Each compartment also has a total volume which is divided into an unstressed and a stressed volume. The unstressed volume is

[2] The equation and parameter values for the model will be supplied by the authors upon request.

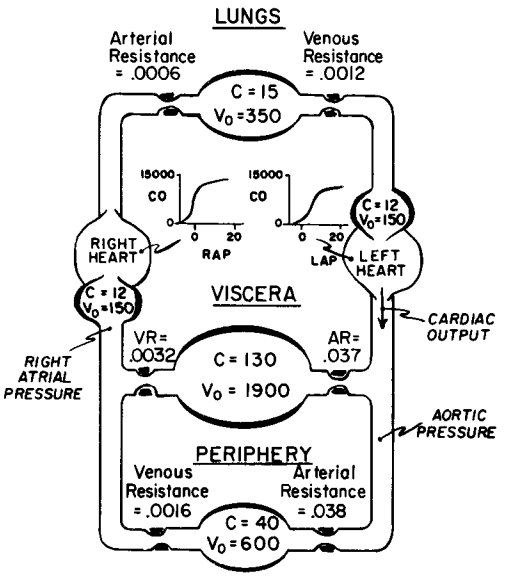

FIG. 1. Schematic representation of the circulation with parallel systemic flow channels.

denoted by V_0 (in ml) and represents the volume of blood at any instant that makes no contribution to the pressure within the compartment. The remainder of the volume is the stressed volume. This volume contributes to the pressure within the compartment according to the formula that pressure is equal to stressed volume divided by the compliance.

A total blood volume of 5000 ml (Guyton, 1971) is initially divided as follows: 70% in the viscera and periphery, 10% in the right and left heart, 10% in the lungs, and 10% left unassigned (Folkow and Neil, 1971). Short term experiments have indicated that approximately 85% of total blood volume is unstressed volume (Richardson *et al.*, 1961). However, stress relaxation should reduce this value somewhat (Prather *et al.*, 1969) and a distribution of 70% unstressed volume and 30% stressed volume was finally selected.

The compliance of the lungs was calculated by dividing the normal stressed volume by a mean pulmonary pressure of 10 mm Hg (Harlan *et al.*, 1967). The combined compliances of the viscera and periphery were calculated by dividing the total stressed volume of these two compartments by a mean systemic pressure of 6 mm Hg (Harlan *et al.*, 1967). This combined compliance was then subdivided, with approximately 75% of the compliance being assigned to the viscera (Caldini *et al.*, 1974; Brooksby and Donald, 1972). Token compliances were assigned to the right and left heart by assuming that these blood storage compartments have a compliance which is comparable to other vessels.

Resistances were calculated from the consideration of normal flows and pressures. The following values were used: mean aortic pressure = 100 mm Hg, right atrial pressure = 0 mm Hg, pulmonary artery pressure = 13 mm Hg, left atrial pressure = 4 mm Hg, and cardiac output = 5000 ml/min (Guyton, 1971). One-half of the cardiac output was assumed to flow through the visceral compartment,

while the other half flowed through the periphery (Caldini *et al.*, 1974). The pressures in the visceral and peripheral compartments were assumed to be 8 mm Hg and 4 mm Hg, respectively (Caldini *et al.*, 1974; Guyton, 1971; Brooksby and Donald, 1972). A relatively high pressure in the visceral compartment is consistent with the idea that blood is stored at a higher average pressure in a portal system because of the "upstream" location of some of the capacitance vessels. The various pressures and flows were then used to calculate the arterial and venous resistances shown in Fig. 1.

Standard function curves were used to describe the pumping ability of the right and left heart (Guyton *et al.*, 1973). Nervous control of the heart and systemic circulation was not included in the model.

Equations representing the model were constructed from the above description and the relationships of Fig. 1. Each of the five blood storage compartments was described by individual parameters, *compliance* and *unstressed volume*, and variables, *pressure* and *volume*, where the volume is the integral of inflow minus outflow. Five flows were calculated from their respective pressure differences and resistances, while two flows were determined by the right and left heart function curves. The value for aortic pressure was calculated algebraically.

The equations were programmed in FOSIL simulation language (Sias and Coleman, 1971) and solved on a Digital Equipment Corporation PDP-9 digital computer. The steady-state values of pressures and flows were very close to the target values described above.

RESULTS

The cardiac output of this model is highly sensitive to changes in venous compliance, and particularly those changes which occur in the visceral compartment. For instance, a 50% increase in cardiac output will result from a 20% decrease in visceral compliance in conjunction with a shift of 20% of the total visceral blood volume from the unstressed to the stressed phase. Changes in cardiac output caused by changes in the properties of the venous blood storage region can be identified by an increase in mean circulatory pressure (Guyton *et al.*, 1973) and are reasonably well understood. The simulations described in the following section, however, will explore additional peripheral factors that might be important in controlling cardiac output. In these simulations, the compliances and unstressed volumes of the circulation will be held constant, while only arterial resistances will be varied. This is a realistic approach in that arterial resistance is known to be one of the most labile of all hemodynamic parameters. The simulations to follow are: (a) dilatation of the visceral arteries, (b) constriction of the visceral arteries, (c) dilatation of the peripheral arteries, and (d) constriction of the peripheral arteries.

Visceral Dilatation. The predicted consequences of visceral dilatation are shown in Fig. 2. There is a precipitous drop in blood pressure associated with an increase in visceral blood flow and a considerable drop in total cardiac output following a decrease in visceral arterial resistance from .037 to .01 mm Hg/ml/min. Peripheral flow, the difference between cardiac output and visceral flow, is severely compromised in conjunction with a translocation of 110 ml of blood from the periphery.

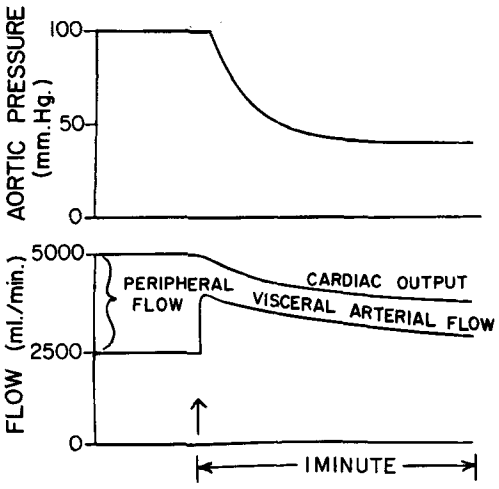

FIG. 2. Hemodynamic response to decreasing visceral arterial resistance from .037 to .01 mm Hg/ml/min. Decrease occurs at arrow.

This translocated blood is much less effective in promoting venous return when it is located in the viscera and both cardiac output and peripheral flow suffer. These results are striking in that we would normally expect an increase in cardiac output following arterial dilatation, rather than a decrease.

A pathological situation bears a striking resemblance to the predictions of the model—the hemodynamic response to the intravenous injection of endotoxins. This response is variable according to the species of experimental animal used, the rate of administration of endotoxin, and other specifics in the protocols used. However, the hemodynamic picture that has developed is one of a precipitous fall in blood pressure to 50 mm Hg or less in conjunction with a less dramatic decrease in cardiac output (Gilbert, 1962; Wyler *et al.*, 1969; Weil *et al.*, 1956; Hinshaw *et al.*, 1961, 1966). Attention has been focused on the visceral circulation in this response because an early, but variable, increase in portal venous pressure is observed, indicating that blood is being pooled in the various organs of the viscera. In addition, the early cardiovascular collapse following endotoxin administration is prevented by evisceration of the animal (McLean and Weil, 1956; Hinshaw *et al.*, 1958). These data have prompted the conclusion that the visceral circulation has responded to endotoxin administration with increased compliance (i.e., dilatation) of the capacitance vessels and increased resistance between the capacitance vessels and the right atrium.

An alternative explanation is that the hemodynamic collapse following endotoxin administration is caused by the dilatation of the visceral arteries, according to the predictions in Fig. 2. In addition to the experimental data summarized above, Wyler *et al.* (1969) and Reichgott *et al.* (1973) have measured the redistribution of blood flow in monkeys following endotoxin administration and have found *increased* blood flow through the viscera at the expense of blood flow through the periphery. Osborne *et al.* (Osborne, M. W., Wenger, J. J., Zanko,

M. T., and Barrett, R. J. Personal Communication, 1973) found no change in mean circulatory pressure in similar experiments in dogs. This data as a whole appears to be more consistent with a simple visceral arterial dilatation than with a combination of increased outflow resistance and increased compliance in the venous region of the viscera. In this regard, increased resistance (i.e., vasoconstriction) and increased compliance (i.e., vasodilatation) may be very difficult to achieve simultaneously in a vascular bed with dimensions of limited lability.

Finally, it has been shown that dextran transfusion (Ebert et al. 1955) helps prevent early circulatory collapse following endotoxin administration and that maintaining blood flow at the normal level by a cardiac assist pump requires an additional 20 cc of blood/kg body weight (Shanbour and Hinshaw, 1963; Weil *et al.*, 1956). If the situation is analyzed using a model with a single flow channel, the data suggest that an increase in compliance has occurred. However, with parallel flow channels transfusion may be necessitated not by increased compliance, but by a blood flow redistribution that causes less effective utilization of a constant compliance divided unequally between the two flow channels. This possibility has been previously mentioned by Caldini *et al.* (1974).

The model's prediction might also correlate with the redistribution of blood flow that occurs during the digestion of food. Increased visceral blood flow and decreased peripheral blood flow have been shown to occur in this situation in conscious dogs (Fronek and Stahlgren, 1968) but in the *absence* of significant changes in either arterial pressure or cardiac output. These animals showed tachycardia during digestion, however, suggesting that the baroreceptor reflexes intervened to help support arterial pressure by peripheral vasoconstriction and visceral venoconstriction (thereby decreasing compliance).

Constriction of the Visceral Arteries. The model predicts that increasing visceral arterial resistance will increase both cardiac output and blood flow to the periphery while decreasing visceral blood flow as shown in Fig. 3. A two and one-half fold increase in visceral arterial resistance produces a 27% increase in cardiac output and 85% increase in peripheral flow in conjunction with a translocation of 220 ml of blood from the viscera to the periphery and an increase in the arterial pressure of 85 mm Hg. These predictions are consistent with the results of Barcroft (1931, 1935), who found that thoracic aortic occlusion produced a 20–30% increase in cardiac output, a doubling of arterial pressure, and a translocation of approximately 16 ml/kg blood from the inferior vena cava to the upper aspect of the dog's body. Stene and Bromberger-Barnea (1971) showed that this same stimulus increased venous return approximately 50% while leaving mean circulatory pressure unchanged.

Recently Caldini *et al.* (1974) analyzed the hemodynamic response to epinephrine infusion and found that the increased cardiac output produced by infusion of epinephrine was due to a combination of decreased venous compliance and a redistribution of blood flow away from the high-compliance venous compartment (i.e., the visceral compartment). These two effects were partially offset by an increase in the resistance connecting the visceral compartment and the right atrium. They concluded that the increase in venous return (and hence cardiac output) would have been negligible without the blood flow redistribution.

The hemodynamic response to exercise also correlates with the predictions shown in Fig. 3. The most dramatic aspect of exercise involves blood flow through the active muscles, and in this model skeletal muscle is part of the peripheral compartment; the dilatation of the peripheral arteries is considered in detail in the next section. However, there is evidence that decreased blood flow through the viscera also plays an important role in the hemodynamic response to exercise. It was first argued by Krogh in 1912 that translocation of blood from the viscera to the periphery would be important in augmenting blood flow through the periphery during exercise. Decreased visceral flow is not necessarily undesirable because both the splanchnic and renal circulation show relatively low arterial–venous oxygen differences. Decreased visceral flow could be compensated for by increased oxygen extraction by these tissues, and hypoxia would thereby be avoided.

In some instances, dramatic decreases in visceral blood flow have been observed during exercise. Bradley (1949) estimated hepatic blood flow in exercising humans using a technique of hepatic extraction of sulfobromophthalein. He found that cardiac output increased 40% and peripheral blood flow increased approximately three fold while hepatic blood flow was *decreasing 40%*. Others (Bishop *et al.*, 1955; Wade *et al.*, 1956; Rowell, 1973) have used similar techniques and have observed that hepatic blood flow decreases to levels ranging from 70% of control to 30% of control during exercise, with Rowell *et al.* (1964) observing a decrease in hepatic blood flow from 1600 ml/min to 500 ml/min during strenuous exercise in humans. Wade *et al.* (1956) observed a 400 ml decrease in estimated splanchnic blood volume during mild exercise in man.

These data suggest that visceral arterial constriction can be a useful adjunct to decreased venous compliance in providing the increased cardiac output needed during exercise. (A similar response, not discussed in this paper, is observed following whole-body heating. See Rowell, 1973.)

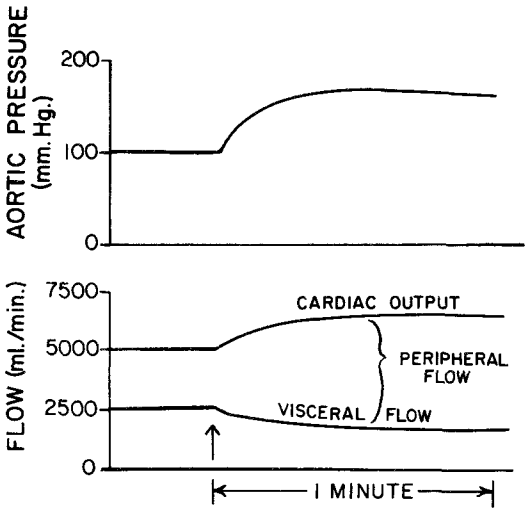

FIG. 3. Hemodynamic response to increasing visceral arterial resistance from .037 to 0.1 mm Hg/ml/min.

Dilatation of the Peripheral Arteries. The model predicts that systemic arterial dilatation will produce an increase in cardiac output, a dramatic increase in blood flow through the periphery, and a substantial fall in aortic pressure as shown by the solid lines of Fig. 4. Peripheral dilatation initially causes a drop in blood pressure from 100 to 40 mm Hg. During the following minute, 280 ml of blood is translocated from the viscera to the periphery causing an improvement in both blood flow and aortic pressure. Aortic pressure eventually rises to 60 mm Hg, cardiac output increases 35%, and blood flow through the periphery is doubled.

Decreased aortic pressure and increased cardiac output also follow arterial dilatation in a single flow-channel model with the fall in pressure being more severe than in the parallel flow-channel model. The parallel flow-channel model shows a greater stability following peripheral dilatation because the blood translocated from the viscera to the periphery is very effective in its new location in promoting venous return and supporting blood pressure. However, both the series and parallel models predict a need for some support of aortic pressure during exercise, and this support can potentially come either from decreased venous compliance or constriction of the visceral arteries as presented in the previous section.

Constriction of the visceral arteries is theoretically very effective in maintaining blood pressure in high flow situations. Visceral artery constriction tends to elevate blood pressure and peripheral artery dilatation tends to lower blood pressure, while both maneuvers promote an increased cardiac output. A more rigorous analysis of combinations of resistance changes will be presented later.

Constriction of the Peripheral Arteries. The model predicts that peripheral arterial constriction will cause an increase in aortic pressure, and a decrease in both cardiac output and peripheral blood flow. A two and one-half fold increase in resistance caused an immediate increase in aortic pressure of 42 mm Hg and an

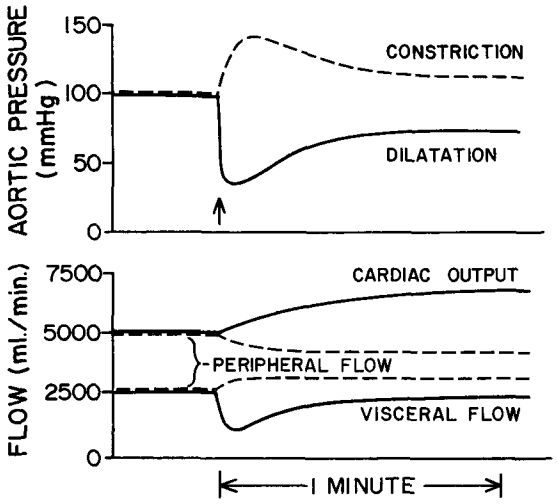

FIG. 4. Hemodynamic responses to decreasing peripheral arterial resistance from .037 to .01 mm Hg/ml/min (solid line) and increasing peripheral arterial resistance from .037 to .1 mm Hg/ml/min (dashed line).

eventual increase of 19 mm Hg. Cardiac output decreased 18% and peripheral blood flow decreased just over 50% in conjunction with a blood shift of 140 ml from the periphery to the viscera.

Experimental correlation comes from the work of Barcroft (1931). He prepared experimental animals in a way that most of the nonvisceral circulation was perfused through the brachiocephalic artery. Occlusion of this artery produced 30–40% increase in arterial pressure and a slight decrease in cardiac output. These results are in good agreement with the predictions of the model, considering that Barcroft's experimental preparation did not completely separate the high venous compliance and low venous compliance blood flow channels. There is little other correlative data available.

Venous Return. The preceding simulations dealt with the relationship of arterial resistance to cardiac output in the *intact* circulation, making the overall response of the model a function of both venous return and the pumping ability of the heart. The effect of changes in arterial resistance on the systemic circulation alone can be more fully understood by studying venous return curves where the function of the systemic circulation is separated from the function of the heart. Figure 5 shows the normal relationship between venous return and right atrial pressure, with the tendency of the blood to return to the heart decreasing as right atrial pressure increases. When right atrial pressure equals mean systemic pressure, blood flow through the systemic circulation stops (Guyton *et al.*, 1973).

Cardiac output is determined by the intersection of the venous return curve and the cardiac function curve, a point that satisfies both the requirements of both the systemic circulation and the heart. In this case the intersection is at a right atrial pressure of zero and a blood flow of 5000 ml per min as indicated by *N*. Changes in venous return can produce different points of intersection.

Venous return curves for the model shown in Fig. 1 were computed for a variety of arterial resistance values by holding the total blood volume in the systemic circulation constant and measuring the blood flow out of the systemic circulation at different right atrial pressures. In the three different venous return curves shown in Fig. 5, there is a linear relationship between venous return and right atrial pressure. Three curves intersect the abscissa at a common value of mean systemic pressure, indicating that venous compliance was not changed during the analysis. An infinite peripheral resistance causes a downward rotation of the venous return curve, while an infinite visceral resistance increases the venous return curve. These changes can occur only in conjunction with requisite changes in arterial pressure, and in particular, constriction of the visceral arteries requires a considerable increase in arterial pressure. The shaded area in Fig. 5 indicates a region of increased venous return (produced solely by visceral arterial constriction) which requires an arterial pressure greater than 200 mm Hg. Because of the finite pumping capability of the heart, extended excursions into this area of venous return can be considered, for all practical purposes, unachievable. It is interesting to note, however, that an upward rotation of the lower, right-hand aspect of the venous return curve can be produced at pressures less than 200 mm Hg. Intersection of the cardiac function curve with this aspect of the venous return curve might occur when cardiac function was severely depressed. Bishop *et al.* (1955) has observed a greater vasoconstriction of the visceral arteries during exercise in

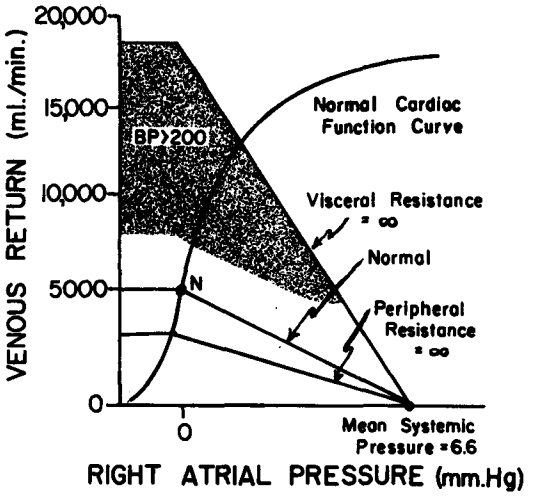

FIG. 5. Venous return curves for the model of Fig. 1. The shaded area represents the region of increased venous return produced by visceral arterial constriction that requires an arterial pressure of 200 mm Hg or greater.

patients with impaired cardiac function. The implication is that these patients had a depressed cardiac function curve and a significant (and beneficial) upward rotation of the venous return curve was possible without requiring impossibly high arterial pressures.

Maximum venous return with graded changes in arterial resistance is shown in Fig. 6. Maximum venous return is defined as the venous return that occurs at a right atrial pressure of zero, with other values of venous return being proportional because of the linearity of the venous return curve. On the abscissa of the figure are the requisite arterial pressure changes that must theoretically accompany excursions in venous return produced by changes in either visceral arterial resistance alone or peripheral arterial resistance alone. These curves indicate that the necessary arterial pressures are frequently intolerably low or impossibly high. The curves in Fig. 6 also show that upward excursions in venous return are theoretically more easily achieved than downward excursions. This is in keeping with the idea that the circulation at rest is at near-minimal flow. Flows significantly below this value are not particularly desirable and the model has good stability in this respect. Flows considerably above normal are desirable in instances such as exercise and the model shows good lability in this respect. The redistribution of blood flow is not contained in this figure, but upward excursions of venous return represent a redistribution of blood flow toward the periphery and downward excursions represent a redistribution toward the viscera.

Figure 6 also shows that solitary changes in either visceral arterial resistance or peripheral arterial resistance are quite likely to produce unacceptable pressure situations without significantly altering venous return. However, if visceral and peripheral arterial resistance are changed in combination, this restriction no longer exists. Figure 7 shows the predicted consequences of several different combinations of visceral and peripheral resistance changes. The arrows denote

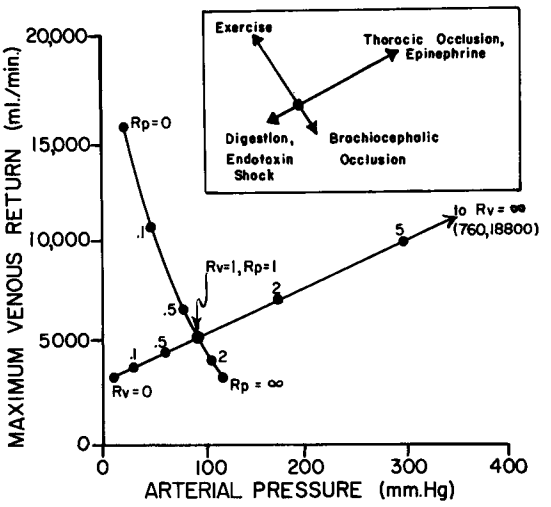

FIG. 6. Sensitivity of venous return and arterial pressure to changes in either visceral or peripheral arterial resistance. MAXIMUM VENOUS RETURN is the venous return that occurs at a right atrial pressure of zero. Numbers adjacent to data points indicate value of resistance (times normal).

excursions away from the normal arterial pressure–venous return operating point. In this instance, a doubling of visceral resistance has been combined with a peripheral resistance (contained in the brackets) ranging from zero, through normal, to infinity. The vertical arrow shows that doubling visceral resistance in combination with decreasing peripheral resistance to .2 of normal will theoretically produce a more than two fold increase in venous return without changing

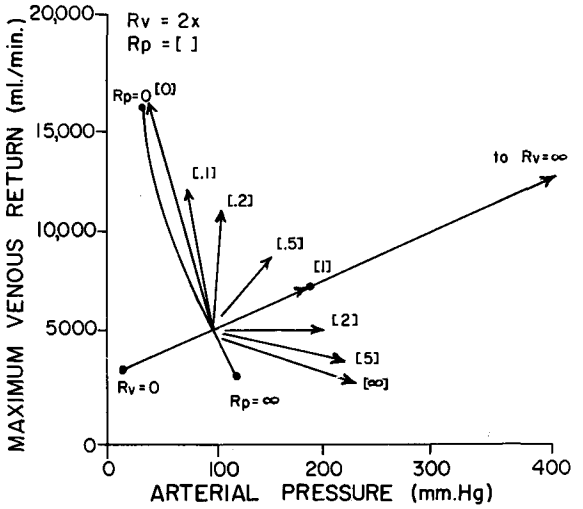

FIG. 7. Excursions of venous return and arterial pressure from normal following a doubling of visceral arterial resistance and various changes in peripheral arterial resistance (shown in brackets).

arterial pressure. On the other hand, other combinations of resistance changes can be more effective in changing pressure than flow. The horizontal arrow shows that doubling both visceral and peripheral resistance will cause a dramatic increase in arterial pressure without changing venous return. The known lability of arterial resistance makes it theoretically possible for a large region of the venous return-arterial pressure surface to be included in the hemodynamic response to various combinations of peripheral and visceral resistance changes.

Limitations of the Model. This analysis was designed to explore only one aspect of the overall control of the circulation; many of the details necessary for a complete description were excluded. Specifically, the predictions of this model relate only to acute or short-term phenomena. Over a longer period of time, autoregulation of blood flow and changes in total body fluid volume will certainly modify or abbrogate the predicted short-term responses. In addition, reflexes might modify the predicted responses, particularly since changes in arterial pressure are such a prominent part of the phenomena.

The mathematical model developed in this study has been designed to focus strictly on *physical factors* within the circulation. Even within this restriction, several assumptions are extremely important. First, arterial resistance and venous resistance were assumed to be constants, unless explicitly changed, and were not a function of distending or transmural pressure. Changes in vascular caliber and resistance following pressure changes could possibly attenuate the predicted responses. For instance, constriction of the visceral arteries will theoretically cause a translocation of blood out of the viscera. Loss of blood from the visceral region will decrease the pressure in this region and this, in turn, could decrease venous caliber and increase the resistance between the visceral blood storage areas and the right atrium. Increased resistance would then oppose the translocation of blood from the viscera and attenuate the total hemodynamic response. In a similar manner, the sensitivity of arterial resistance to changes in arterial pressure could also modify the total hemodynamic response. Secondly, this mathematical analysis has not considered the importance of arterial compliance. Changes in the amount of blood stored in the arteries in response to changes in arterial pressure and arterial compliance would also participate in the total hemodynamic response. In short, this analysis is intended to isolate and emphasize a single aspect of the overall control of cardiac output.

CONCLUSION

The mathematical analysis presented here explores the changes in cardiac output that can theoretically be produced in a circulatory system having two parallel blood flow pathways with dissimilar venous compliances. It is well known that changes in cardiac function and venous compliance can produce dramatic changes in cardiac output, and the response of this model to those stimuli is not significantly different than that of other models. However, a model with two parallel flow channels has some unique properties; in this study, attention was focused on the hemodynamic response to individual changes in arterial resistance in the visceral and peripheral blood flow pathways.

The results of these analyses are consistent with results obtained by Krogh at the turn of the century using less experimental data and simpler analytical tools. The primary conclusion is that redistribution of blood flow can cause a translocation of blood; the blood is then more or less effective in promoting venous return in its new location according to the values of venous compliance and resistance at the new location. Significant changes in venous return can theoretically be achieved by changes in arterial resistance which are quantitatively realistic.

This paper does not argue that changes in arterial resistance should be considered a substitute for changes in venous compliance in controlling cardiac output. However, recent data obtained from electromagnetic flow measurements and radioactive microspheres has emphasized that the redistribution of blood flow is an important aspect of many hemodynamic responses. In this regard, the consequences of redistribution could be a useful adjunct to changes in venous compliance in the overall control of cardiac output. For instance, the model predicts that visceral artery constriction in combination with peripheral artery dilatation would be a very effective means of increasing venous return in exercise.

The consequences of changes in arterial resistance need not be beneficial. The model also predicts that hemodynamic collapse follows visceral artery dilatation, a response that bears a striking resemblance to the hemodynamics of endotoxin shock.

We conclude that regional distribution of blood flow is potentially very important to the control of cardiac output and, subsequent to further experimental verification, these concepts may be useful in understanding many common hemodynamic situations.

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