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A critical analysis of the view that right atrial pressure determines venous return

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Abstract

A C Guyton pioneered major advances in understanding of cardiovascular equilibrium. He superimposed venous return curves upon cardiac output curves to reveal their intersection at the one level of right atrial pressure (Pra) and flow simultaneously consistent with independent properties of the heart and vasculature. He showed how this point would change with altered properties of the heart (e.g., contractility, sensitivity to preload) and/or of the vasculature (e.g., resistance, total volume). In such graphical representations of negative feedback between two subdivisions of a system, one input/output relationship is necessarily plotted backwards, i.e., with the input variable on the "y" axis (here, the venous return curve). Unfortunately, this format encourages mistaken ideas about the role of Pra as a "back pressure", such as the assertion that elevating Pra to the level of mean systemic pressure would stop venous return. These concepts are re-examined through review of the original experiments on venous return, presentation of a hypothetical alternative way for obtaining the same data, and analysis of a simple model.

Keywords

cardiac output, cardiovascular equilibrium, mean systemic pressure, peripheral vasculature, vascular function curves

A critical analysis of the view that right atrial pressure determines venous return

We owe to A.C. Guyton and co-workers major steps toward the understanding of the mechanical coupling between the heart and the peripheral vasculature. Their experimental data, described graphically as "venous return curves" (Fig. 1) revealed how right atrial pressure (Pra) varied in relation to the rate of flow through the peripheral vasculature (2, 5, 6). Guyton went on (2) to combine this new information with extant information about the relationship between Pra and cardiac output. He pointed out that the dependence of cardiac output on Pra and the functional relationship shown in a venous return curve together dictate an equilibrium in the intact system at a specific Pra and cardiac output. He illustrated the equilibrium graphically as the point of intersection of the appropriate cardiac output curve with the appropriate venous return curve, each appropriate in the sense of representing specified states of the heart and vasculature, respectively. He also focused on the pressure recorded with zero flow through the vasculature, defined as mean systemic pressure (Pms), seeing Pms as manifesting the total volume contained within the peripheral vasculature in relation to the elastic properties of the complex container comprised by the peripheral vasculature.

The value of this approach to studying the cardiovascular system cannot be overestimated; the work of Guyton, et al., set the stage for the intervening decades of progressive expansion of knowledge about control of cardiac output (12). Yet, some have misinterpreted features of venous return curves as applicable to analysis of the *dynamics* of venous return. Indeed, "venous return" implies a dynamic context. We would not need this separate term except for those situations in which cardiac output and venous return temporarily differ. In fact, Guyton, et al., did not record venous return in dynamic states. They emphasized that their data were all taken from *steady states* (5).

Therefore, a physical model based on the sloped segment of venous return curves cannot apply to dynamic states. In that model, taught to three generations of medical students, venous return is driven through a fixed hydraulic resistor connected between a pressure source fixed at Pms and an independently variable "back pressure" Pra. Clinicians and physiologists discuss venous return dynamics in these terms; the extreme example being the statement that elevation of Pra to Pms would stop venous return. This practice of taking the components of the model as having actual counterparts in the vasculature confuses a mathematical abstraction with reality.

In the hope of clarifying this issue, this paper begins with review of how venous return curves were obtained, followed by brief discussion of features of the curves. Then, alternative ways of recording the relationship

between Pra and venous return are discussed, including a hypothetical one. In this "thought" experiment, the experimental preparation differs slightly from the one employed by Guyton, et al., to make it, perhaps, easier to see the consequence of maintaining fixed blood volume and to illustrate dynamic versus steady-state conditions. Finally, the issue of mathematical abstraction versus reality is discussed in terms of a simple physical model.

How venous return curves were obtained

Preparation and apparatus

Guyton and his colleagues obtained the data for their venous return curves through the ingenious use of a Starling resistor to manipulate Pra without altering the amount of volume circulating in the peripheral vasculature. Their preparation, illustrated schematically in Fig. 2, is described in various papers; for a detailed description, see the 1957 paper (5).

Venous return was conveyed from a cannula in the right atrium (outflow via the tricuspid valve was occluded) to the suction line of a pump via a Starling resistor. The tubing connections between the resistor and the cannula and the resistor and the pump were flexible so that the resistor could be moved up and down. A blood reservoir was connected to this external plumbing but the connection was shut off during data acquisition so that the volume of blood contained within the peripheral vasculature remained constant for all the data points of a given venous return curve.

The outflow from the pump was routed to the pulmonary artery. The authors emphasized that the left ventricle faithfully pumped out cardiac output at exactly the rate that flow was pumped into the pulmonary artery.

Their data on venous return were obtained from a single flowmeter on the *outflow* side of the pump. They had no way of discriminating between cardiac output and venous return. They were justified in describing their flow data as venous return only in that *cardiac output and venous return were identical for every data point recorded*.

The Starling resistor functioned as a variable resistance in the connection between the right atrial cannula and the inflow port of the pump. This device was essentially a short length of large-bore thin-walled flaccid rubber tubing. Resistance to flow of a Starling resistor depends upon its intramural pressure profile. When intramural pressure is well above atmospheric pressure all along the length of the resistor, the tubing is distended and offers little resistance to flow. However, if intramural pressure falls below atmospheric pressure, the tubing is compressed rather than distended and resistance to flow is greatly increased.

When the conditions of flow and pressure profile are such that a Starling resistor is in a partial state of

collapse, i.e. distended at the upstream end and compressed at the downstream end, one can conclude that intramural pressure is equal to atmospheric pressure just upstream of the point where narrowing begins. Guyton et al. employed this indication to set the level at which pressure in the tubing system equaled atmospheric pressure.

To alter Pra, they adjusted the height of the Starling resistor relative to heart level, keeping the resistor in a state of partial collapse. Pra was therefore established by the length of the hydrostatic column between the level of the resistor and the level of the atrium; subatmospheric if the resistor were positioned below heart level, and vice versa.

Procedure

Note in Fig. 1 that flow was highest at low Pra. The authors emphasized that Pra was kept at −8 mm Hg or lower most of the time to promote as much venous return as possible (5) to forestall deterioration of the preparation. Data were recorded at the end of brief periods (8-10 seconds) during which the Starling resistor was elevated to obtain desired levels of Pra. Before and after these periods, which were just long enough for flow and pressures to reach a new steady state (in their terms, after "an equilibrium rate of flow had been established", reference 5, p. 610), the resistor was positioned below heart level to return to the starting subatmospheric Pra.

Necessity of changes in pump output

As shown in Fig. 1, blood flow through the vasculature fell during the periods of elevated Pra. Therefore, we know unequivocally that the outflow rate from the pump was reduced during these periods, because the flowmeter was on the pump outflow line.

What changed pump output is not clear in the 1957 paper (5). Elsewhere, descriptions of the same experiments specifically mention that the operators adjusted pump output. One paper refers to adjustment of pump output to maintain pressure at the pump end of the Starling resistor within a specific range of subatmospheric pressures (pg 189 in reference 4). Another refers to controlling right atrial pressure "… by increasing or decreasing the minute capacity of the pump …" (pg 125 in reference 2). These can be interpreted (see p 744 in Levy's critical review, reference 8) to mean that the operators manually adjusted the pump after each elevation of the Starling resistor to obtain the desired state of partial collapse of the resistor tubing. However, it is conceivable that the throttling action of the Starling resistor determined pump output.

Note that the pump consisted of a series of closely spaced mechanical fingers, side by side, that pressed on a length of flexible tubing in succession to create a kind of peristaltic action. Its output would have depended upon

the rate of sequencing of the fingers and also upon how completely the tubing filled between compressions. Pump output would have been reduced if high resistance of the Starling resistor resulted in pressures in the supply line of the pump so low that the tubing would fail to fill during the fill cycle.

Obligatory redistributions of volume associated with altered Pra and flow

Why the Starling resistor would at least temporarily have greater resistance to flow and why pump output had to fall after elevation of Pra can be better understood through consideration of the change in distribution of the blood volume necessarily associated with change in Pra.

With the Starling resistor placed well below heart level (solid lines for peripheral vasculature and connections to Starling resistor in Fig. 2), the great veins close to the right atrium were not fully distended, i.e. the volume contained within this segment of the vascular container was relatively low because the transmural pressures were low.

Having less volume in one segment means that the reciprocal amount of blood has been transferred to other segments. Accordingly, the solid lines suggest that, with less of the total blood volume in the vessels near the right atrium, more of it is upstream.

The dashed lines suggest the distribution of volume when the Starling resistor was positioned above heart level, when higher pressures in the vicinity of the right atrium obligated greater distention of the affected vessels, made possible through transfer of volume from upstream segments of the vasculature.

These different distributions of volume are necessarily associated with different rates of flow. For example, when Pra was increased and blood accumulated within the central conduit veins to distend them sufficiently to bring pressures into equilibrium with the new Pra, the volume that accumulated had to come from compliant segments of the vasculature upstream. For that to happen, pressures in those upstream segments had to fall. In order for pressure in upstream segments to fall, *pump rate had to fall*, allowing decline in pressure in the aorta and throughout the segments upstream of those that became relatively distended after the increase in Pra.

This conclusion depends upon the constraint that total volume contained within the peripheral vasculature remained constant. Other necessary restrictions include that regional compliances did not change, that flow was not redistributed among the parallel organ vasculatures, and that no other energy sources (muscle pumping, respiratory pumping) were coupled into the vasculature.

Note the consequence for the Starling resistor of the volume dynamic initiated when it was elevated from

the level that kept Pra subatmospheric during the rest periods. During the subsequent moments of diversion of venous return to distention of the large veins, the rate of inflow into the resistor would have been correspondingly reduced. Meanwhile, the rate of outflow was initially, at least, still at the high level set by the pump during the preceding rest period. Thus volume within the resistor tubing itself would have been reduced, increasing the tendency to collapse and obstruct flow with the consequence of reducing pressure in the inflow line of the pump. Collapse and perhaps fluttering of the resistor tubing would have been visual evidence of the need to adjust pump output. Alternatively, these changes in the Starling resistor might have sufficiently restricted inflow to the pump to reduce output to the level commensurate with the new level of Pra.

What the sloped segment of classical venous return curves tells us

It makes no difference to the arguments of this paper whether pump output was adjusted manually or throttled by the Starling resistor. What matters is recognition that steady state Pra and the rate at which of blood passes through the peripheral vasculature are locked in a functional relationship. For each height of the Starling resistor, pump output had to settle at the cardiac output that would create the distribution of volume and pressure that would allow Pra to stabilize at the new level dictated by the height of the hydrostatic column.

Zero intercept of the sloped segment: mean systemic pressure

The point at which the linear sloped segment intercepts zero flow is defined as mean systemic pressure (Pms). For critical review of this concept and of mean circulatory pressures, related to the volume of the entire cardiovascular system as opposed to that of the isolated vasculature, see Rothe (9, 10).

The horizontal segment

Guyton, et al. (5) found that the Starling resistor could be positioned arbitrarily far below heart level with no change in flow, giving the series of data points for sub-atmospheric Pra (Fig. 1) at nearly constant flow described here as the horizontal segment of a venous return curve. This was interpreted as the consequence of partial venous collapse, i.e. the great veins functioned as Starling resistors and isolated upstream pressures from influence of progressively more negative Pra.

Alternative ways of acquiring data on the relationship between right atrial pressure and venous return

The relationship between Pra and steady state flow through the vasculature discovered by Guyton and his co-workers has been reproduced in independent laboratories and with different methodologies (1, 7, 8).

Matthew Levy's vascular function curves

In particular, Matthew Levy (8) published data from experiments with a right-heart bypass preparation identical to that employed in the Guyton laboratory except that the Starling resistor was omitted. He set pump output at particular levels and recorded Pra.

Over the range of pump output from zero through maximal, he observed progressive decline of Pra. He was not able to record a wide range of sub-atmospheric Pra at the upper limit of cardiac output because, without a Starling resistor to create ever more negative Pra, he could only drive Pra down to the level associated with the maximal level of output.

Since Levy manually adjusted flow, it was natural to see Pra as the dependent variable and plot it on the y-axis – the format Levy referred to as a "vascular function curve". With this point of view, the natural focus falls upon the steady state cardiac output pumped through the vasculature as the determinant of Pra.

A "thought" experiment

What goes on in the collection of data for a venous return curve can perhaps be understood more clearly if we imagine using a preparation nearly identical to that employed by Guyton, et al (Fig. 2). In this hypothetical preparation (Fig. 3), the tubing conveying the venous return is allowed to overflow into a reservoir rather than connecting to a Starling resistor. The pump that forces flow through the peripheral vasculature is supplied from this reservoir rather than from the outflow of the Starling resistor. Further imagine that the peripheral vasculature under study is the one characterized by the venous return curve illustrated in Fig. 1.

The objective is to reproduce the data of Fig. 1. Because a given venous return curve is associated with a specific fixed volume, this requires setting the volume contained within the vasculature to the same level as in the original experiment, call it Vo. To do this, the hypothetical experiment begins with the open end of the venous return tubing positioned at a height above heart level that corresponds to a hydrostatic pressure of 6.5 mm Hg at the right atrium, equal to Pms in the original experiment. We turn on the pump to obtain a cardiac output in the normal range, wait for equilibration between cardiac output and venous return, and then shut off the pump. Venous outflow continues briefly and comes to a stop with the venous return tubing full to the brim. Now, Pra is 6.5 mm Hg and pressure is equilibrated with Pra everywhere throughout the vasculature. This is mean systemic pressure, Pms.

With Pms at 6.5 mm Hg, the same zero-flow pressure illustrated in Fig. 1, we know that the intravascular blood volume is at Vo.

Next set the pump at, say, 1 liter•min^{-1}. Almost immediately, venous return begins to spill out of the tubing at an increasing rate until it steadies at 1 liter•min^{-1}. Pra remains at 6.5 mm Hg, set by the so-far unchanged height of the end of the tubing (Fig. 4).

We now have a steady state data point for pressure and flow (1 liter•min^{-1}, 6.5 mm Hg) but it *does not belong on the venous return curve* we have set out to obtain -- volume is now greater than Vo. Why? Because elevated pressures in each vascular segment obligate proportional volume increases. Before starting the pump, the pressure profile around the vascular circuit was flat, equal everywhere to 6.5 mm Hg. Forcing flow through the vasculature caused elevated pressures, ranging from a maximum in the aorta (Pao) down to 6.5 mm Hg in the right atrium (Fig. 4). The increase in total intravascular volume above Vo would have been apparent as the accumulation over time of the difference between the outputs of the two flowmeters (shaded area A in Fig. 4), or, more simply, by the reciprocal decrease in volume of the supply reservoir.

To get rid of the excess volume, we lower the tubing end bit by bit (pump rate is still set at 1 liter•min^{-1}). With each decrement in Pra, the rate at which flow spills out of the tube temporarily rises before it stabilizes again at 1 liter•min^{-1}. That temporary excess of venous return occurs because of the volume that leaves segments of the vasculature as they passively recoil to equilibrate with the new reduced distending pressures (with no change in total peripheral resistance and fixed flow, the difference (Pao – Pra) is fixed, so, ignoring effects of vessel diameters on resistance, pressure falls by the same amount over the entire profile, as illustrated in Fig. 4). When all of the excess volume has been removed, Pra is necessarily at 4 mm Hg, the pressure associated with Vo and a steady-state flow of 1 liter•min^{-1} in Fig. 1.

Successive upward adjustments of pump output and subsequent searches (incremental lowering of the tubing end) for the level of Pra that brings systemic volume back to Vo would map out the identical relationship between Pra and flow shown in the sloped segment of the venous return curve in Fig. 1.

The phenomenon that causes the horizontal segment of a venous return curve can also be explored. In the sequential progression of upward adjustments of pump output followed by lowering the tubing to bring volume back to Vo, the tubing would eventually be set to a level, below the heart, at which negative pressures in the large conduit veins immediately upstream of the right atrium causes them to collapse partially. Any further reduction of Pra has no influence on the pressure profile upstream; it only causes further collapse. With no transient increase in venous return due to passive volume removal, no change in pump output is necessary to correct volume back to Vo, no

matter how much we lower Pra.

The hypothetical experiment could equally well have been carried out with a sequence of changes in Pra and subsequent adjustments of flow to reestablish volume at Vo. Either way obtains the same pressure:flow relationship (Fig. 1) determined by the physical properties of this particular vasculature at Vo because of the immutable functional relationship between flow and Pra. Fig. 5 illustrates the dynamics associated with elevation of Pra. As the tubing end is raised, volume accumulates during the temporary disparity between cardiac output and venous return (shaded area A); downward adjustment of pump output is necessary to restore volume to Vo. Only in this rather backward sense is venous return determined by Pra. Clearly, it is the pump that causes the steady state pressure profile.

In these sequential steady states with volume at Vo, the greater the flow, the steeper the overall pressure profile (Fig. 5) because the pressure gradients along the resistive elements of the vasculature in the areflexive preparation must increase with flow. In the redistribution of Vo with each increase of flow, pressure increases in arterial segments are much greater than the decreases in Pra and venous system because the arterial segments are less compliant. Therefore, the point in the pressure profile where pressure equals Pms moves further upstream. Clearly, Pms does not have a physical counterpart as a fixed pressure reservoir at the upstream end of a fixed resistance to venous return.

Venous return curves are not about venous return as distinct from cardiac output

To sum up, this paper offers absolutely no dispute against the validity of the obligatory relationship between steady state flow through the vasculature and Pra under conditions of fixed systemic volume discovered by Guyton, et al. (5). What it disputes is the idea that "venous return" curves describe venous return as distinct from cardiac output.

That they do not is revealed by study of the original papers. The authors clearly point out that data were obtained in steady states. The graphical presentations of the data could as legitimately have been named something like "dependence of pressure at the outflow of the peripheral vasculature upon cardiac output" though it might not then have seemed natural to have Pra on the x axis.

Unfortunately, selection of the term "venous return curve" and of the format of the graphic evokes the misleading idea that, in the vascular subdivision of the cardiovascular system, Pra somehow determines venous return. It is true that a given level of Pra, over the range of the sloped segment, is necessarily associated with the

corresponding level of flow, but it is not the cause, it is the effect. The thought experiment described above reveals that it is no more possible to turn around the drive and response sides of this relationship than it is to make the relationship between preload and cardiac output operate in reverse.

Nonetheless, the approach pioneered by Guyton (2) of superimposing venous return curves upon cardiac output curves is a convenient way to look at the negative feedback interaction between the major subdivisions of the cardiovascular system (Fig. 6).

Utility of plots of the Pra:cardiac output relationship in descriptions of the negative feedback interaction between the heart and the vasculature

Cardiac output curves, as applied by Guyton in his Physiological Review article (2) describe the influence of preload, expressed as Pra, on cardiac output under conditions of fixed heart rate, afterload, and contractility. Just as different venous return curves are plotted for different levels of systemic volume or different vasomotor states, families of cardiac output curves are used to illustrate influence of altered contractility or afterload.

Cardiac output curve data are obtained in the "open-loop" configuration, i.e., Pra is controlled independent of how the pressures in the vasculature are affected by the resultant cardiac output. So are venous return curve data, i.e., they describe the isolated vasculature, independent of any consequences of altered Pra on cardiac function. Putting these two functional relationships together should enable describing the closed loop steady-state equilibrium point of the intact cardiovascular system (Fig. 6). This was the advance contributed by Guyton's technique of superimposing cardiac output curves and venous return curves, (Fig. 7). He made it easy to visualize consequences of changes in cardiac function or of properties of the systemic vasculature for equilibrium cardiac output and Pra (2).

An equally meaningful graphical approach would be to overlay cardiac output curves on plots of vascular function in the format of Levy's vascular function curves (8), illustrated in Fig. 8. To do that, the cardiac output curves must be plotted with cardiac output on the x-axis. That will look backwards to many, since the idea that it is preload that influences cardiac function, not vice versa, is ingrained.

But, plotting the relationship in the vasculature between Pra and cardiac output in the format of a venous return curve is no less backward. Whenever two systems interact in a negative feedback connection like the interaction between the heart and the vasculature illustrated schematically in Fig. 6, a graphical illustration that overlays their separate open-loop input-output properties necessarily shows one plotted "backwards".

Models of the vasculature that predict the sloped segment

This paper does not dispute that the linear approximation of the sloped segment of a venous return curve

for a particular volume is the pressure:flow relationship that would occur if venous return were driven by a fixed Pms and variable Pra, respectively at the upstream and downstream ends of a fixed resistance. What it disputes is taking this model as having real counterparts. This misconcept arises from a mathematical abstraction; the sloped segment appears this way because of the redistribution of a fixed total volume within the vasculature at different flow rates, not because there is a reservoir with pressure fixed at Pms.

Guyton and his co-workers certainly did not propose a two-pressure, one resistor arrangement as a model of the peripheral vasculature . They worked with networks of resistances and capacitances (6) intended to approximate properties of anatomically identifiable segments of the peripheral vasculature. From these, they derived quantitative solutions that adequately explained the sloped segment of venous return curves.

Indeed, they showed that the apparent resistance indicated by the slope did not correspond to a physical resistance of any particular segment of the vasculature. In terms of the model, it could be identified as a composite of resistance and capacitance properties of the entire circuit. For example, in Chapter 13 of his 1963 monograph (3), Guyton specifically describes the apparent resistance as a combination of arterial resistance and arterial and venous capacitances of the system as well as venous resistance. Elsewhere the term "venous impedance", was used (6).

For simulations that come closer to accurate prediction of the dynamics of the peripheral vasculature including the consequences of regional vasomotor adjustments, more complex representations of properties of the vasculature are necessary; see, for example Tsitlik et al., (15). But simple models like the one used by Guyton et al., (6) and the one Levy used in his critical review (8) suffice to show what underlies the obligatory decline in right atrial pressure with increase in flow revealed in venous return curves.

A simple model adequate for prediction of sloped segment data

Models are not attractive if their components cannot be recognized as having counterparts in the system to be described. The model illustrated in Fig. 9 is perhaps the simplest possible first approximation of peripheral vascular mechanics. It is not offered as a new model for vascular dynamics, only for illustration of points about the significance of (Pms – Pra) that seems apparent in a venous return curve.

Overall vascular compliance is divided into three compartments in the belief that the flow-dependent distribution of volume is not adequately explained by reciprocal transfer between one arterial compartment and one venous compartment (especially in situations where arterial pressure is kept constant). One of the venous compartments corresponds roughly to the venular segments of the organ microvasculatures, the other to the major

collecting veins. For an introduction to this view of properties of the venous system, see Rowell (11).

In the mechanical representation of the model in Fig. 9, the relative size of the peripheral venous system is drawn to suggest the high distensibility of the venular segments of the venous system compared to lower compliances of the other compartments. The segments between the compliant compartments represent the hydraulic resistances of the arterial and venous systems.

Flow is pumped into the circuit and removed from the downstream end at identical rates, in accord with the finding of Guyton, et al. (5) that changes in pulmonary volume were negligible when pump output changed. Venous return is the flow passing through the venous resistor. In this model it differs from pump output (cardiac output) for the brief periods during which pressures and volumes in the compliant compartments readjust after changes in pump rate.

The schematic in the lower section of Fig. 9 shows an arrangement of electrical components analogous to the mechanical model. The analogous relationships are: electrical current as blood flow, electrical resistance as hydraulic resistance, voltage as pressure, electrical capacitance as compliance, and charge as volume. Total charge in the system, the sum of the voltage•capacitance products for each compartment, represents the total volume contained within the vasculature, taken as 6000 ml. Values chosen for Ca, Cpv, and Ccv were taken, respectively, as 5, 80 and 15% of a total vascular capacitance estimated for a 70 kg human as 175 ml• $(mmHg)^{-1}$. Values chosen for the resistors between compartments were 20 and 0.87 (mmHg) •$liter^{-1}$•min, respectively, for Ra and Rv.

As an aside, capacitors do not accurately represent compliant vascular compartments that contain volume at zero distending pressure, i.e., “rest” or "unstressed" volume. However, mean systemic pressure can be modeled through initial conditions of charge stored in the circuit. For network elements that represent the complex non-linear properties of compliant segments of the vasculature, see Tsitlik et al. (15).

The circuit is driven by a pure current source. It removes current from the right atrial end at exactly the same rate that it forces current into the arterial end.

With the current (blood flow) set at zero, voltages (pressures) equilibrate, i.e. Pa = Ppv = Pra, at a level that depends upon the total charge (representing fixed system volume) set as an initial condition. Charge distributes among the capacitors in proportion to their capacitance. This uniform voltage and distribution of charge is the analog of the zero-flow situation in which mean systemic pressure, Pms, is seen. References to analogous quantities, henceforth, will be in terms of blood flow, pressures and volume.

At any other level of blood flow, the development of pressure gradients causes increased volume in the arterial capacitor matched by an equal decrease in the total volume in the venous capacitors. This volume distributes between the two venous capacitors according to the pressure profile set by flow rate. Changes in flow change the differences between Pa and Ppv and Ppv and Pra, dictating progressive decreases in Pra with progressive increases in flow.

The electrical circuit is readily analyzed with the aid of computer simulation. For particular values of compliance and resistance chosen to represent a 70 kg human, Pra is predicted to vary with flow as shown in Figs. 10 and 11. Fig. 10 shows the details of how Pra changes in time after each adjustment in flow. Fig. 11 shows the pressure:flow relationship plotted with Pra on the vertical axis (Levy's vascular function curve format, reference 8). Data from the simulation, plotted as a solid line closely agree with data points taken from the venous return curve of Fig. 1.

Note that arterial pressure necessarily rises in proportion to flow in this model with fixed arterial resistance as it did in reality in experiments of Guyton, et al., (5) with areflexive dogs and in the experiment described by Levy (8). The volume in the arterial compartment increases progressively with cardiac output; calculated values of arterial pressure for flow rates of 1 and 5 liter•min^{-1} are 26 and 102 mm Hg, respectively. Both venous compartments supply volume that moves to the arterial compartment, declining from the volume each held with pressure at Pms. The relationships between compartment volumes and flow are illustrated in Fig. 12. The increase in arterial volume with flow reflects the progressive increase in arterial pressure with each increment in flow; decreases in the volumes of the two venous compartments accompany decreases in pressure and combine to equal the reciprocal decrease in volume

An interesting variation appears if the model is revised to allow for adjustment of the arterial resistor so that arterial pressure remains constant, as if perfectly controlled via the baroreflex. Simulations were repeated for flow levels below 5 liter•min^{-1} (but not to zero, in deference to the impossibility of maintaining arterial pressure when flow approaches zero) with arterial resistance values selected to put arterial pressure at 102 mm Hg, the same as the 5 liter•min^{-1} pressure in the fixed arterial resistance simulation. Dashed lines in Figs. 11 and 12 join the predicted data points. Note that the slope (apparent resistance) of the Pra:flow relationship differs, (solid versus dashed line in Fig. 11) and that extrapolation of the dashed line in Fig. 11 would underestimate Pms.

In the simulations with arterial pressure held constant over a range of cardiac output, volume in the arterial

compartment does not change (Fig. 12). Consequently, for the lower flow levels, the combined volume of the venous compartments is relatively low. The net result is lower pressures in each compartment.

Something like the difference illustrated by the separation of the solid and dashed lines in Figs. 11and 12 must occur in reality. Yet, Guyton et al. made a point of close correspondence between curves obtained regardless of whether the animal had intact reflexes (5). This issue is unresolved.

What the math tells us about the apparent role of mean systemic pressure in the sloped segment

The highly simplified model of Fig. 9 is sufficient to reveal the obligatory relationship between right atrial pressure and cardiac output seen in the sloped segment of experimentally obtained venous return or vascular function curves. It predicts a flow:pressure relationship consistent with the idea that flow in the sloped segment is driven by (Pms - Pra) through a fixed resistance. We can see why by manipulating the equations that describe the circuit, beginning with the relationship between total blood volume, V, and the pressure:capacitance products for each compartment (additional symbols are defined in Fig. 9):

$$V = PaCa + PpvCpv + PraCcv$$

This is combined with expressions for Pa and Ppv in terms of steady-state flow, F, and pressure differences with respect to Pra:

$$Ppv = Pra + RvF$$

$$Pa = Pra + RvF + RaF$$

This can be put in the form:

$$F = (Pms – Pra)/Req$$

by incorporating the definition of Pms:

$$Pms = V/(Ca + Cpv + Ccv)$$

In this formulation, the "equivalent" resistance, Req, is indeed the negative reciprocal of the slope in a plot of flow versus Pra and we see the flow indeed follows the relationship to Pra and Pms seen in the sloped segment of a venous return curve. But Req *is not equal to the venous resistance in the circuit*. Rather:

$$Req = (RaCa + RvCa + RvCpv)/(Ca + Cpv + Ccv)$$

This expression for Req is similar to the “impedance to venous return” derived by Guyton, et al., (6). Like a Thevenin equivalent in electrical circuit theory, it does not correspond to an actual resistance. It is a composite of the actual physical components of the network. Note that Req can approximate the value of Rv, the representation

of venous system hydraulic resistance, if arterial system capacitance is close to zero and if the compliance of the peripheral venous system is much larger than that of the central venous system. That does not justify regarding flow as driven by a fixed pressure, Pms, at the upstream end of Rv. Doing so overlooks the simple fact that the pump is the energy source that forces flow through the vasculature and establishes a different profile from aortic down to right atrial pressure for each level of flow.

True, the three-capacitor two-resistance model analyzed here inadequately represents the real vasculature. It is far more inadequate to consider dynamics of venous return in terms of a variable Pra opposing a fixed Pms. That amounts to representing the vasculature by a two-compartment, one-resistor model with components selected merely because they are mathematically consistent with the slope and intercept of the sloped segment.

Note that, though a three-compartment model adequately predicts the sloped segment of venous return curves, it does not consider energy sources besides the pump, particularly the pumping action of respiratory and skeletal muscles. It is therefore useless for explaining the radical alteration of the relationship between cardiac output and right atrial pressure in exercise, when an important share of the total mechanical energy expended in forcing flow through the vasculature comes from the pumping action of skeletal muscle contractions. Of interest in this regard are recent studies in which investigators took on the daunting objective of recording Pra in an intact animal in relation to cardiac output during exercise. These revealed that a reciprocal relationship between total flow and right atrial pressure is still seen when cardiac output is changed at a fixed level of exercise (13, 14) .

Summary

Guyton et al. (2, 5, 6) solved the problem of how to study the relationship between the steady-state rate of blood flow through the peripheral vasculature and right atrial pressure (Pra) without the complication of changes in total intravascular volume. They presented their data in the format of venous return curves (Fig 1), with Pra on the horizontal axis.

Alternative ways of obtaining the flow:Pra relationship (8) as well as a “thought” experiment presented here reveal the fallacy of taking their findings to say that Pra governs venous return through the hydraulic resistance of the venous system as a back pressure acting against mean systemic pressure (Pms) on the other end of the resistance. In the original experiments, it was the reduction of output that enabled Pra to come into equilibrium with the levels set by elevating their Starling resistor. What venous return curves really show is the steady-state relationship between rate at which blood flows through the vasculature and Pra plotted “backwards”, i.e., with the

independent variable on the "y" axis.

Cardiovascular equilibrium occurs through the negative feedback interaction between the subdivisions of the system – increasing Pra increases cardiac output in the cardiac part; increasing cardiac output reduces Pra in the vascular part (Fig. 6). Guyton introduced the technique of superimposing plots of these "open-loop" relationships to reveal the one point simultaneously consistent with both of them and therefore the point of equilibrium cardiac output and Pra. In this graphical technique, one relationship is necessarily plotted "backwards" (Figs 7 and 8).

During brief periods when venous return and cardiac output are not identical, but total vascular volume is fixed, the difference is made up by reciprocal exchange of volume between compliant compartments (in a broader view than the focus in this paper, these include the pulmonary vasculature and chambers of the heart). We can describe such transients by reasoning out how the pressure profile changes when flow changes and how volume is thereby redistributed or, in a more advanced view, how pressure profiles in the parallel organ vasculatures change when cardiac output changes with arterial pressure constant. Or, we can take a quantitative approach with the aid of simple models like the one in Fig. 9 or more sophisticated ones with better description of the components and their interconnections (15).

The equations that describe the steady-state behavior of simple models can be manipulated into a form showing flow equal to (Pms – Pra)/Req, consistent with the proportional relationship seen in the sloped segment of a venous return curve. However, the apparent resistance, Req, is a composite of all the resistances and capacitors of the model, Pms does not remain constant at the upstream end of one of the resistors, and the expression does not apply to situations in which it is meaningful to speak of venous return as distinct from cardiac output.

Allowing the formality that steady-state venous return can be described as proportional to (Pms – Pra) to suggest that this two-pressure, one-resistance model has some correspondence to the actual dynamics of venous return is worse than an over-simplification. It overlooks the fact that it is the cardiac pump (together, in the real world, with the pumping action of skeletal and respiratory muscles) that supplies the mechanical energy that creates the pressure profile through the vasculature.

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Figure Legends

Fig. 1.

A venous return curve. Data points (open squares) were scaled from Fig. 5 in Guyton, et al. (5) from the representative curve for humans. Arrow points to pressure defined as mean systemic pressure (Pms).

Fig. 2.

Symbols: RA, right atrium; LV, left ventricle. Adapted from a sketch contributed by Loring B. Rowell to illustrate schematically the physical arrangement of the preparation and apparatus employed by Guyton et al (5). Dashed versus solid lines for the circuit between the left ventricle and right atrium suggest the altered distributions of the blood volume within the peripheral vasculature associated with high versus low right atrial pressure.

Fig. 3.

Hypothetical re-plumbing of external connections illustrated in Fig. 2 to obtain identical venous return curve data. Instead of connecting to a Starling resistor, the tubing from the entrance to the right atrium (A) is left open, positioned so that venous return spills into the reservoir below. Blood is pumped from the reservoir into the pulmonary artery (B). A second flowmeter is added for direct recording of venous return.

Fig. 4.

Initial step in hypothetical experiment. Upper panel: after a period with flow at zero and tubing height set to put Pra at 6.5 mm Hg and intravascular volume at Vo, pump output is brought to 1 liter•min^{-1}. Volume, represented by shaded area A accumulates until venous return equilibrates. As level of tube end is lowered, volume is brought back to Vo (shaded area B represents net accumulation of excess venous return). Lower panel: steady state pressure profiles i.e., descent from aortic pressure (Pao) to right atrial pressure (Pra): At zero flow, pressure in all segments is Pms. Solid line: elevated profile that obligates volume expansion with the pump at 1 liter•min^{-1} and Pra still at 6.5 mm Hg. Dashed line: profile after lowering Pra.

Fig. 5.

Upper panel: dynamics of adjustments between steady states before and after a change in Pra. Initially, venous return and cardiac output are identical, Pra is steady, intravascular volume is at reference level, Vo; then Pra is increased by elevating height (h) of open tubing end; finally, pump rate is decreased to allow volume to return to Vo. Shaded areas A and B show accumulation of volume and subsequent reduction during transient changes in venous return.

Lower panel: steady-state pressure profiles, i.e., descent from aortic pressure (Pao) to right atrial pressure (Pra): initial (solid); after increase in h (upper dashed); final, after flow reduction (lower dashed).

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Schematic negative feedback relationship between main subdivisions of the cardiovascular system. Other things being equal, increase in Pra causes increased cardiac output in the cardiac subdivision; increase in cardiac output causes decreased Pra in the vascular subdivision. Stability occurs at the single point consistent with the two separate relationships.

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A cardiac output curve, i.e. the dependence of cardiac output on Pra (dashed) for fixed levels of contractility, afterload, and heart rate, superimposed upon the data from Fig. 1. Note that the y axis for flow rate is labeled as cardiac output, appropriate for both relationships.

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Two versions of a model of the peripheral vasculature, mechanical above and electrical below. Voltages at the nodes in the electrical circuit represent pressures (Pa, arterial, Ppv peripheral venous, Pra, right atrial) with the zero pressure reference indicated by the ground connection to zero voltage. Capacitors Ca, Cpv, and Ccv correspond to compliances of the three compartments. The pump that forces flow (F) through the peripheral vasculature is represented by a current source.

Fig. 10.

Predicted Pra from the model in Fig. 9. Note that arterial pressure increases with each step up in pump output in this simulation.

Fig. 11.

Solid line: the relationship between steady state levels of Pra and pump output from Fig. 10, plotted in the format of a vascular function curve. Open squares are the data points from Fig. 1, except that flow data are scaled for 1.7 m^2. Dashed line: the relationship obtained when the arterial resistance is adjusted for each level of flow to

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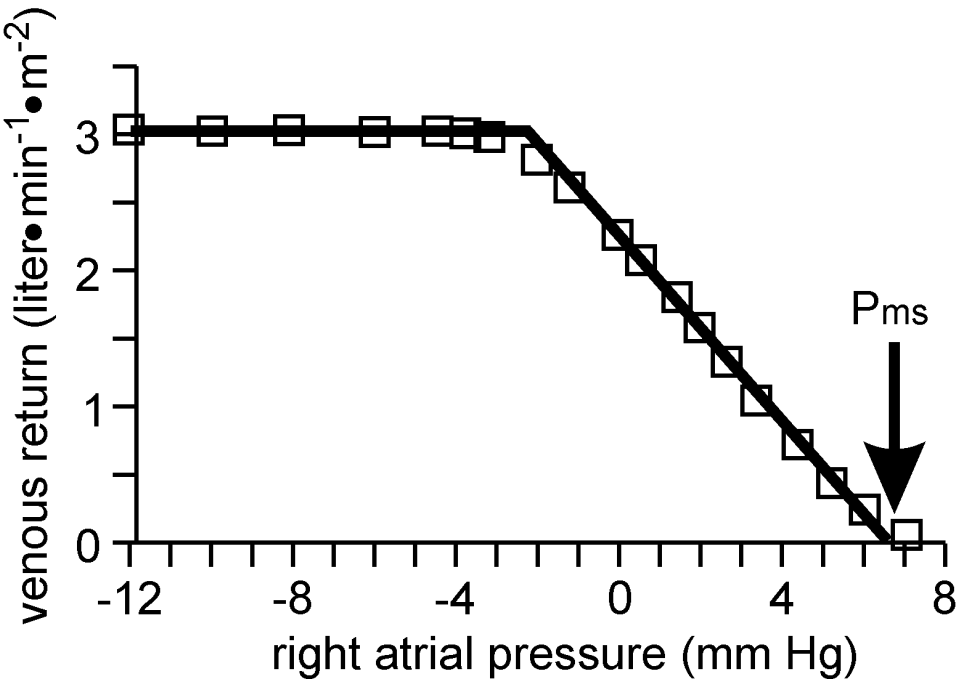
Compartment volumes relative to compartment volume at zero distending pressure, from the simulations illustrated in Figs. 10 and 11. Solid lines, simulation with constant arterial resistance; dashed lines, simulation with constant arterial pressure.



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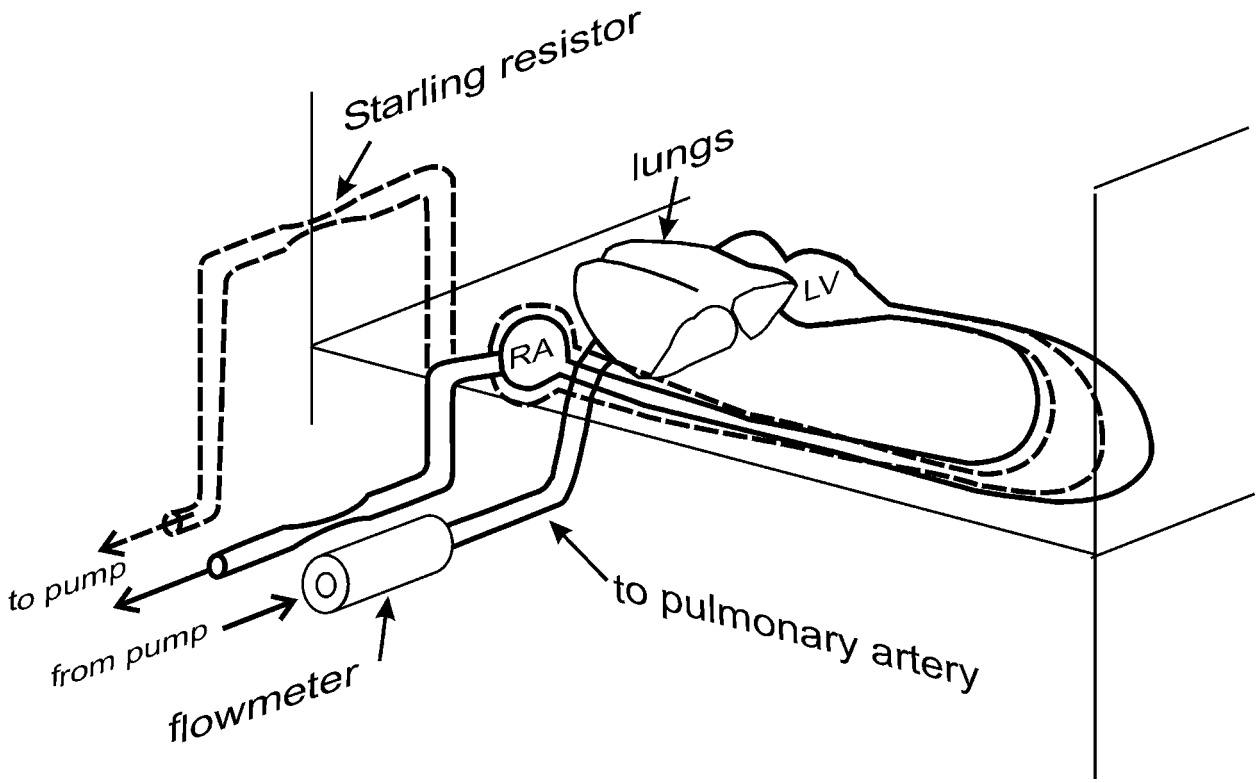

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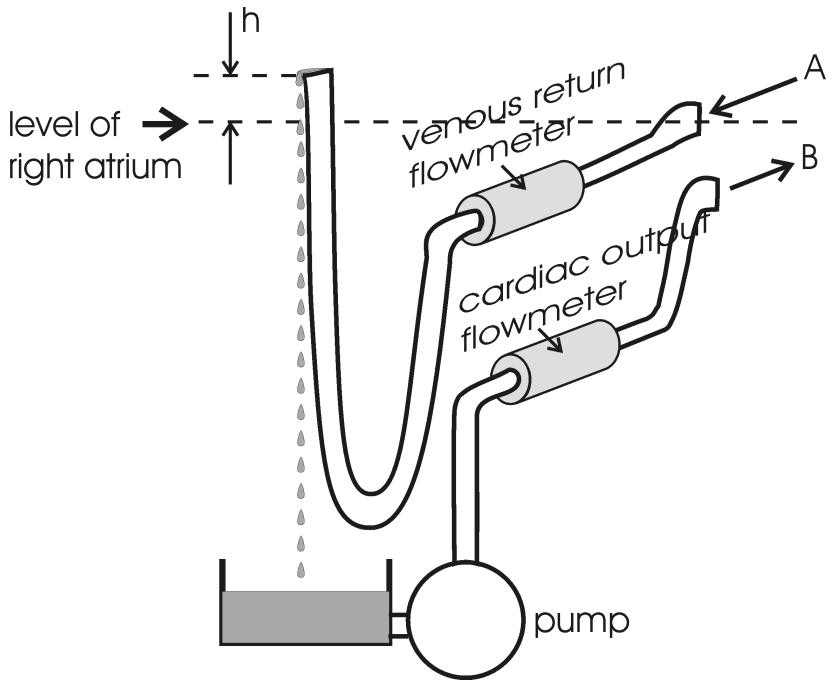

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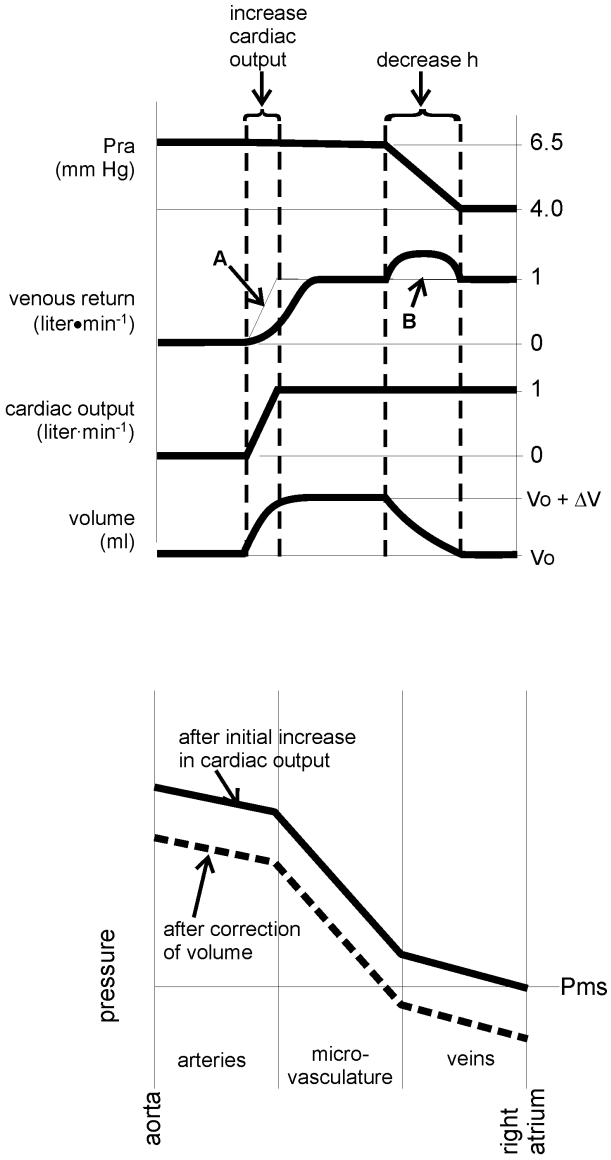

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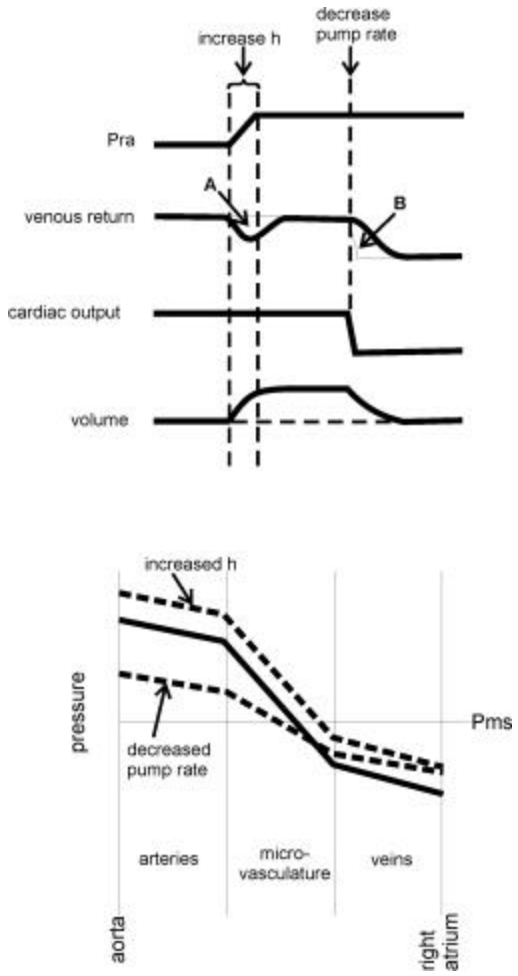

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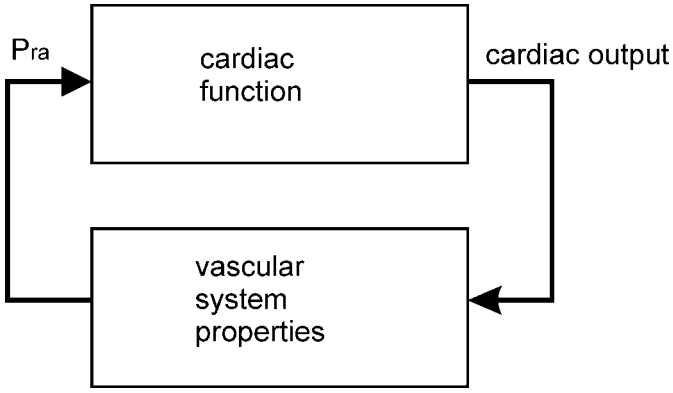

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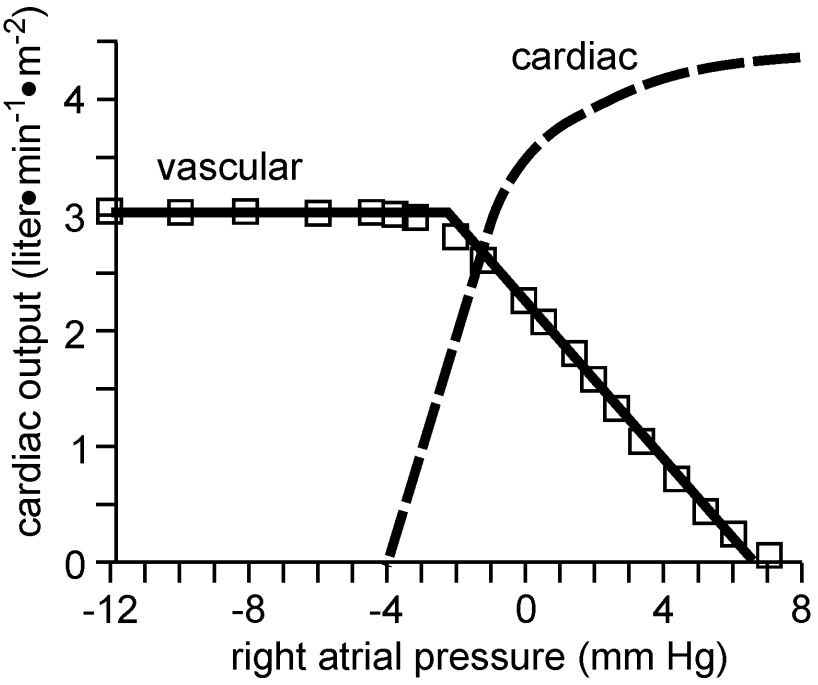

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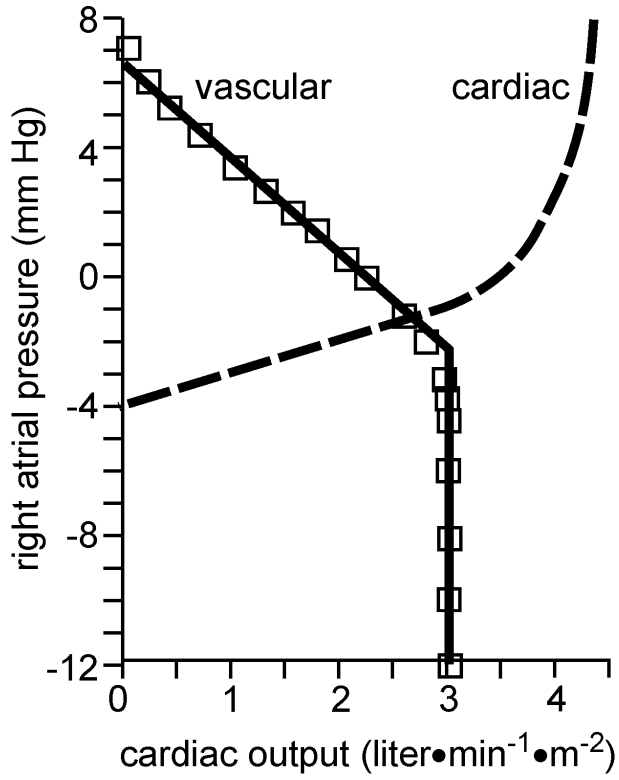

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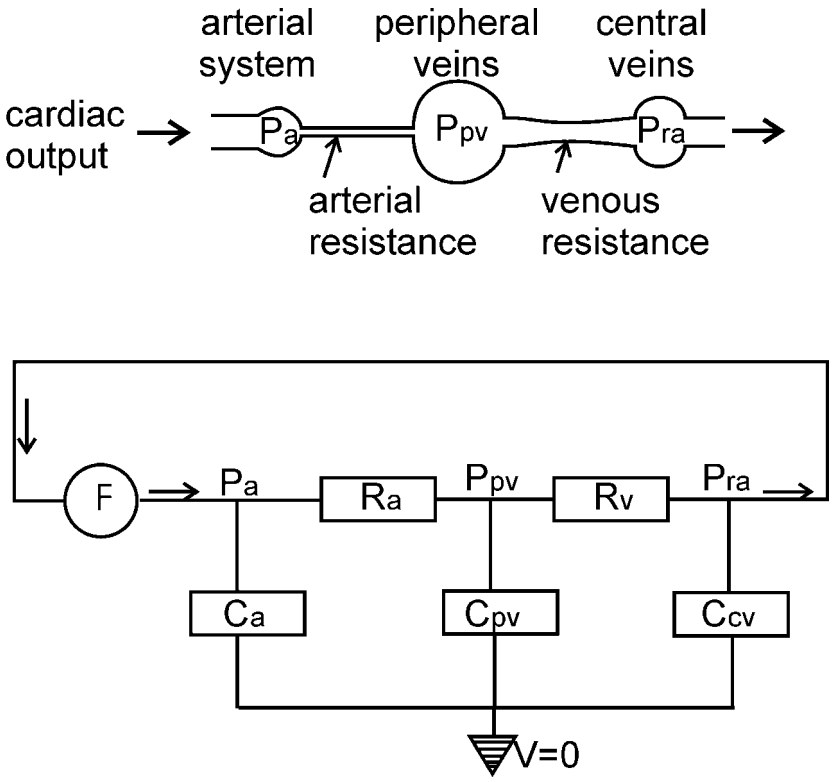

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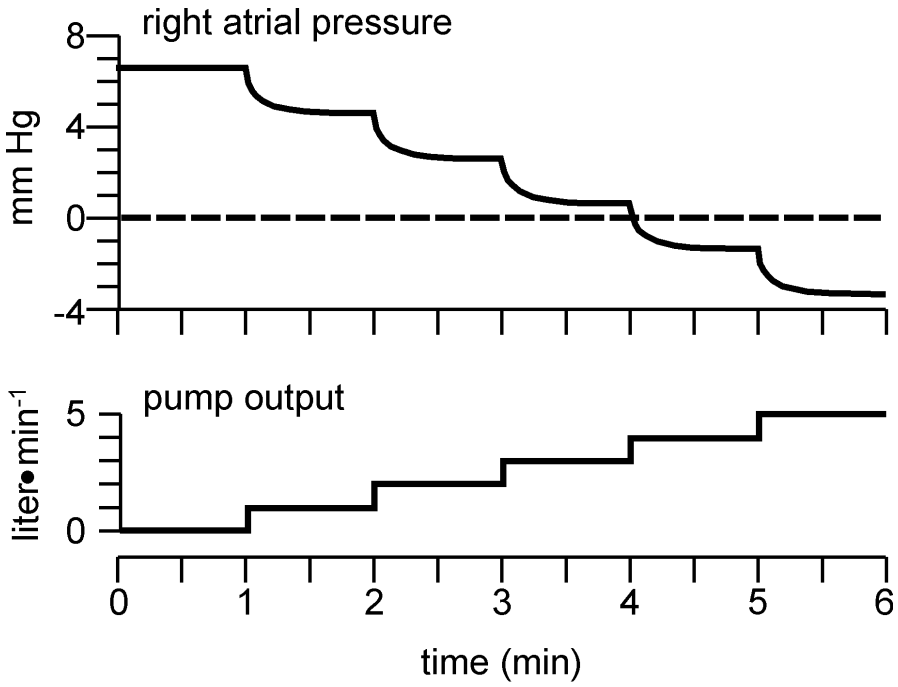

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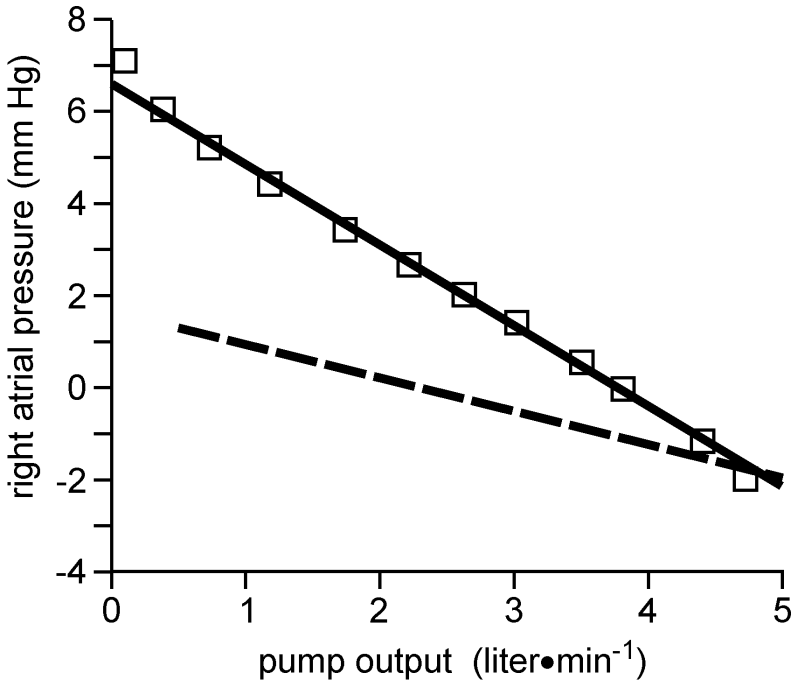

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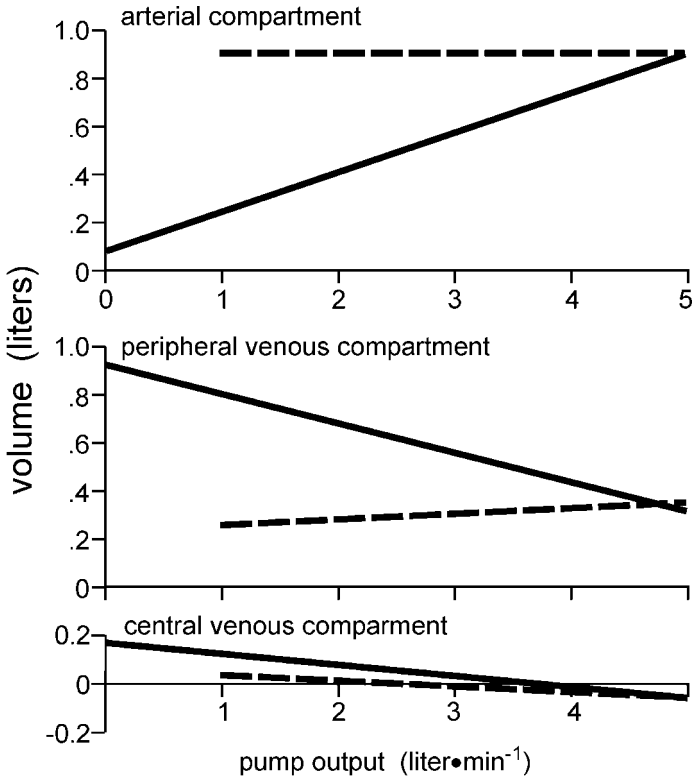

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