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Point:Counterpoint: The classical Guyton view that mean systemic pressure, right atrial pressure, and venous resistance govern venous return is/is not correct

PURPOSE AND SCOPE OF THE POINT:COUNTERPOINT DEBATES

This series of debates was initiated for the *Journal of Applied Physiology* because we believe an important means of searching for truth is through debate where contradictory viewpoints are put forward. This dialectic process whereby a thesis is advanced, then opposed by an antithesis, with a synthesis subsequently arrived at, is a powerful and often entertaining method for gaining knowledge and for understanding the source of a controversy.

Before reading these Point:Counterpoint manuscripts or preparing a brief commentary on their content (see below for instructions), the reader should understand that authors on each side of the debate are expected to advance a polarized viewpoint and to select the most convincing data to support their position. This approach differs markedly from the review article where the reader expects the author to present balanced coverage of the topic. Each of the authors has been strictly limited in the lengths of both the manuscript (1,200 words) and the rebuttal (400). The number of references to publications is also limited to 30, and citation of unpublished findings is prohibited.

POINT: THE CLASSICAL GUYTON VIEW THAT MEAN SYSTEMIC PRESSURE, RIGHT ATRIAL PRESSURE, AND VENOUS RESISTANCE GOVERN VENOUS RETURN IS CORRECT

What makes the blood go around? This must be one of the most fundamental questions in cardiovascular physiology. It at first seems intuitively obvious that the heart must be the primary source of energy. Indeed it has been argued that the pressure gradient from the aorta to the right atrium determines the flow (14, 24, 25). However, it is evident that the pressure generated by the heart bears no relationship to total flow in the system (13). For example, cardiac output can increase more than five-fold during exercise with only moderate changes in arterial pressure and double in septic patients with a fall in blood pressure. Arthur Guyton advanced our understanding of the determinants of steady-state blood flow by analyzing the dual roles of right atrial pressure (Pra): *1*) as the determinant of the filling of the right heart in Starling's law of the heart and *2*) as the back pressure to the blood flow from the circuit (3).

A key element in Guyton's analysis is the role of the elastic recoil pressure of the circuit. The flow of water out of a bathtub provides a useful analogy for understanding the role of this elastic force (15, 19). The rate of emptying of a bathtub is determined by the height of water above the bottom and the drainage characteristics of the tube draining the tub, which include the resistance to flow and downstream pressure. Inflow from the tap only affects outflow by increasing the height of water in the tub. Importantly, the force or pressure coming out of the tap does not affect outflow, only the volume filling the tub provides the "elastic" energy for emptying the tub. When the tub is filled, the initial rate of emptying through the drain is the same whether the tap is on or off.

Similarly the volume that fills and stretches the elastic structures of the vasculature produces a pressure that provides the potential energy for the system. This pressure is determined by the volume and total compliance of the vasculature and is called mean systemic filling pressure (MSFP). Its importance was first recognized by Weber in the 19th century (see Refs. 3 and 26) and later by others (2, 9). Total vascular compliance is determined by the sum of the regional compliances. Venules and veins contain ~70% of blood volume at a low pressure and thus their compliance (Cv) dominates the characteristics of the vasculature and acts much like a bathtub.

When the pressure downstream of a bathtub is the same as the pressure in the tub, the tub does not empty. Similarly, when the pressure downstream to the venules and veins (i.e., Pra) is equal to MSFP, there is no flow. Flow only occurs when Pra is lowered relative to MSFP. The heart has two roles in this process. Cardiac contractions lower Pra and allow greater emptying of the circuit. Second, the heart provides a crucial "restorative" force. That is, it pumps the blood back into the systemic circulation and maintains the initial elastic recoil pressure. Of importance, the heart cannot significantly increase MSFP. This is because the volume that the heart pumps comes from the region of MSFP and there is no other substantial source of volume that the heart can use to augment MSFP except for small amounts from the pulmonary circuit and large veins (21).

Guyton showed that the return of the blood to the heart (VR) is approximated by the equation $VR = (MSFP - Pra)/Rv$, where Rv refers to the cumulative resistance in the venous system (12). Steady-state cardiac output must equal VR and visa versa and the overall flow from the heart is regulated by adjustments in the mechanical characteristics of the circuit and the heart (18). Because Pra is the determinant of venous return that is regulated by the heart, it is appropriate to consider Pra as the independent variable for venous return when venous resistance, compliance, and stressed volume are constant. Accordingly, Arthur Guyton developed his very elegant graphical analysis of the interaction of cardiac and return function by placing Pra on the *x*-axis and flow on the *y*-axis (Fig. 1; Ref. 10).

Veins have floppy walls and collapse when inside pressure is less than outside pressure, which produces what is called a vascular waterfall (23). Normally collapse occurs around atmospheric or "zero" pressure and when "waterfall" conditions are present further decreases in Pra do not increase flow. Thus for a given set of circuit conditions, the maximal possible cardiac output occurs when Pra is ≤ 0. The heart also produces a limit to cardiac output when the plateau of the cardiac function curve is reached (17). As Guyton termed it, the heart determines "permissible" flow (11).

This allows an appreciation of the significance of the potential energy from the volume in the venules and veins. If the circulation is arrested and the veins are disconnected from the heart and allowed to drain to atmospheric pressure, there is

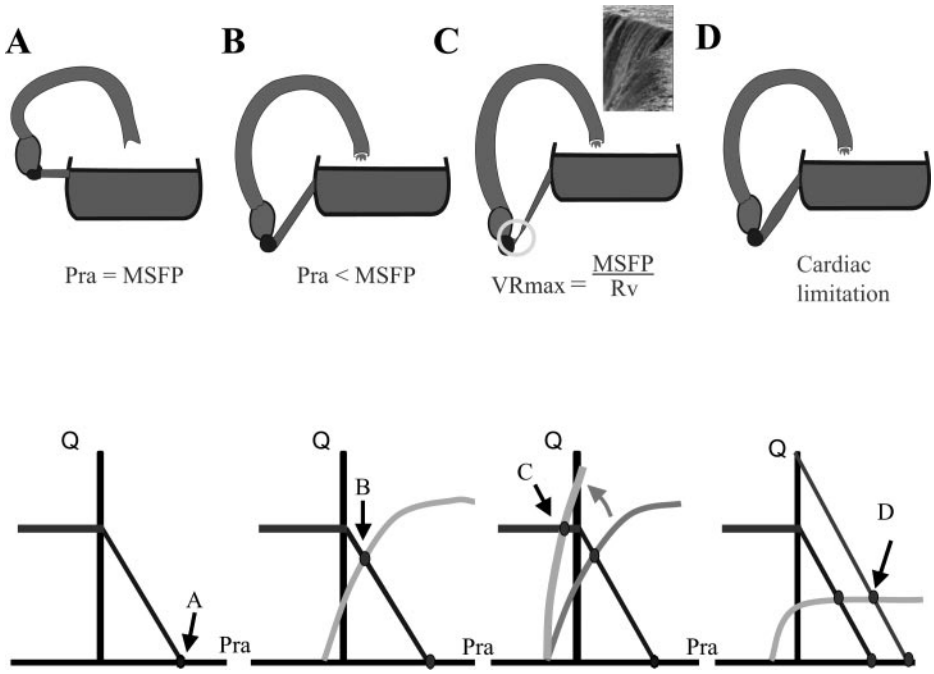

Fig. 1. Schematic model of the circulation and graphical analysis of the interaction of cardiac function and return function. *A*: right atrial pressure (Pra) equals mean systemic filling pressure (MSFP) and flow is zero. *B*: cardiac function curve intersects the return function and the 2 define the operating cardiac output, the venous return and the Pra. *C*: Pra is <atmospheric pressure and venous return is maximal ("waterfall" condition); increases of cardiac function in this range do not increase cardiac output ("return limited"). *D*: the return curve intersects the plateau of the cardiac function curve so that an increase in the return function does not increase cardiac output ("cardiac limited").

immediate flow, which is the maximal possible for the system. This maximal possible flow occurs without a heart and the heart can only get in the way by giving a Pra >0 (22)! Obviously this maximal flow is very transient, for the elastic recoil energy is rapidly dissipated and the energy must be "restored" by the work of the heart. Maximum possible flow in the system is determined by stressed volume divided by the time constant of its drainage, which is given by Rv × Cv.

The effects of small changes in downstream pressures are very evident in experimental preparations in which venous return and cardiac function are disconnected (4–8, 20). In these experiments, the vena cavae are cannulated and drain through "y" connectors, which create vascular waterfalls. Blood drains into a reservoir and is pumped back into the animal at a fixed flow rate. Adjusting the height of the y connectors can regulate venous outflow pressures. Raising the y connectors produces an immediate fall in outflow, which then returns to a new steady state after volume accumulates in the upstream vessels and increase the regional MSFP. The converse occurs when the y connectors are lowered as long as venous pressure is greater than atmospheric pressure. By design, inflow remains constant. It might be expected that the arterial pressure would rise with the increases in venous pressure (1), but it does not. This is likely due to a Starling resistor-like mechanism at the level of the arterioles, which produces an arterial vascular waterfall (16) so that regional increases in MSFP do not affect arterial flow until they exceed the waterfall pressure. The presence of a Starling resistor further strengthens the argument that the forward force from the heart does not directly regulate venous flow and arterial inflow behaves like a tap in a bathtub.

In conclusion, cardiac output is determined by the interaction of cardiac function and return function. The volume filling the compliant vessels of the vasculature provides an elastic recoil pressure, which is the major source of energy for the flow of blood to the right heart. Pra acts as a backpressure to this flow, and the heart can regulate cardiac output by regulating Pra. The heart also restores the volume that drains from the systemic circulation and maintains MSFP.

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S. Magder
Division of Critical Care Medicine
McGill University Health Centre
Montreal, Quebec, Canada
e-mail: sheldon.magder@muhc.mcgil.ca

COUNTERPOINT: THE CLASSICAL GUYTON VIEW THAT MEAN SYSTEMIC PRESSURE, RIGHT ATRIAL PRESSURE, AND VENOUS RESISTANCE GOVERN VENOUS RETURN IS NOT CORRECT

How mean circulatory pressure (Pms) and right atrial pressure (Pra) influence venous return (Fv) in relation to resistance of the venous system (Rven) is commonly discussed in terms that imply the balloon-like physical model illustrated in Fig. 2. The model supports characterization of Pra as a "back pressure" and assertions such as pointing out that elevating Pra to equal Pms would stop venous return (6).

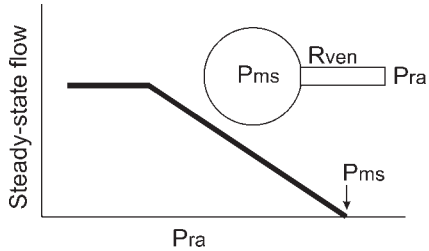

Fig. 2. Mean circulatory (Pms) and right atrial (Pra) pressures as the pressure gradient driving venous return. Implicit in typical discussions of the influence of Pra on venous return is a balloonlike model like the *inset* shown with inside pressure at Pms; a resistive outflow path representing venous resistance, Rven; and pressure at the outflow end at Pra. Outflow from the balloon would obey the relationship (Pms−Pra)/Rven. *Provided that Pms were held constant*, this expression would also describe the sloped portion of the graph of the relationship between steady-state flow and Pra, an idealized "venous return curve."

This view of Pra as the determinant of Fv in proportion to its decrement relative to Pms, which I will call the (Pms−Pra)/Rven concept, is an interpretation of findings of Guyton et al., presented in venous return curves like that in Fig. 2 (many publications by Guyton and his coworkers address our subject; for background citations, see Ref. 1). My argument is that the interpretation is wrong.

To begin with, the balloon model has a glaring defect. It would not generate the steady flow associated with any level of Pra below Pms in the venous return curve because outflow would remove volume from the elastic compartment. Inside pressure would fall along with volume according to the compliance of the compartment. Outflow rate would decline accordingly as the elastic energy stored in the compartment walls was expended. To keep Pms constant would require a pump, but then the drive for Fv comes from the pump, not stored elastic energy manifested as Pms.

Stored elastic energy was not what propelled the flow recorded for venous return curves like that in Fig. 2. Flow came from a pump whose output, recorded as Fv, passed into the aorta of the peripheral vasculature under study. The only way to change Fv was by manually resetting the pump rate or by throttling the pump by imposing a resistance in the connection to its inflow port.

Return flow was intercepted at the right atrium (where Pra was recorded) and fed through a Starling resistor to the input end of the pump. The Starling resistor functioned as a variable resistance that throttled the pump, thus changing pressures and volumes throughout the vasculature until Pra settled at the value consistent with the height of the hydrostatic column between the level of the resistor and the level of the right atrium. The beauty of this closed-loop design was that they could keep the volume contained within the vasculature constant while recording a range of steady-state levels of Fv and corresponding Pra by adjusting the height of the resistor (see, for example, Ref. 4).

So, Fv was certainly not the outflow of an elastic compartment shrinking in volume, it was recorded when flows, pressures, and segment volumes throughout the vasculature were steady.

Also, in no way was venous return recorded as distinct from the rate at which flow entered the aorta. In the investigators' view, cardiac output would be the flow seen by an observer in the aorta looking upstream. Venous return would be what the observer would see if he turned around and looked downstream, the same flow, but in the opposite sense.

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Writers have stressed that one cannot say Pra or Fv is the independent variable in the intact cardiovascular system (e.g., Ref. 6). The same is true of the Starling resistor + peripheral vasculature + pump system. But, when we open loops, we can identify independent and dependent variables unequivocally. Remove the Starling resistor, find some other way of keeping total circulating volume constant, and you can independently set Fv at various levels in an isolated peripheral vasculature and observe what happens to Pra [as various workers have done, e.g., Levy (5)]. Obviously, you cannot do the opposite;

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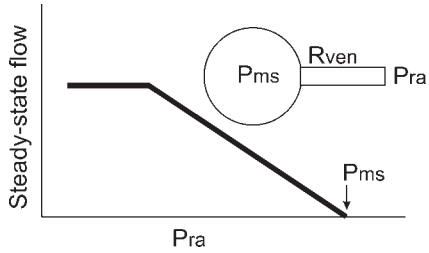

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Fv is the independent variable in the Fv:Pra relationship in the isolated vasculature. Without a pump, you can set Pra wherever you want but you will get no steady-state flow.

My dispute is with the (Pms−Pra)/Rven concept, not the significance of the experimental results. Knowing how Pra changes in relation to steady-state flow passing through the vasculature as an open loop subsystem of the cardiovascular system with Fv as the independent variable enabled an important advance. Guyton put this new information together with cardiac output curves [properties of the open loop cardiopulmonary subsystem, with Pra as input and flow, Fco, as output, (2)]. By doing this graphically, he could discuss steady-state equilibrium points for the closed-loop system in terms of changes in either subsystem, such as the overall elevation of a venous return curve with increased system volume.

In this technique, both open-loop relationships are plotted on one graph. Guyton chose to put flow on the *y*-axis and pressure on the *x*-axis. That meant that the peripheral vasculature dependence of Pra on Fv ended up plotted as in Fig. 2, i.e., with the independent variable on the *y*-axis. Unfortunately, the apparent proportionality between (Pms−Pra) and Fv plus the mistaken idea that Pra was actually the independent variable launched the (Pms−Pra)/Rven concept.[1]

Perhaps two other considerations contributed to persistence of the concept. *1*) (Pms−Pra)/Rven appeals to those with a Poiseuillean view who look for a pressure gradient as the cause of flow through a vascular segment and overlook the fact that pressure gradients and flow in the vasculature develop hand in hand as a consequence of pumping. *2*) The elastic compartment in the physical model in Fig. 2 has an intuitive appeal because of the importance of stored elastic energy in driving venous return as understood in the following sense. The appropriate reason for a separate term for "venous return" as distinct from "cardiac output" is that the rates at which blood is pumped into the aorta and at which flow returns to the right atrium can differ temporarily. These transient discrepancies involve transfers of elastic energy and changes of vascular volumes beyond the predictive capability of a pumpless one-chamber model.

Why then does Pra fall below Pms in proportional relation to flow? Not because Pms is a fixed pressure head at the upstream end of a fixed venous resistance, but because progressively greater flow creates a progressively steeper pressure profile around the peripheral vasculature. With no flow, pressure in all segments of the vasculature is Pms. Forcing flow through the vasculature elevates arterial pressures above Pms. Total blood volume is fixed, so the volume that expands arterial segments is displaced from venous segments where pressures therefore fall below Pms. It is this progressive reallocation of total volume among the elastic segments of the vasculature that results in decline in Pra proportional to flow.

So what does drive venous return? In the isolated peripheral vasculature setting of venous return curves, it is set by a pump. In the closed-loop cardiovascular system, it equilibrates with cardiac output at a level set by variables such as total system volume, contractility, and elastic state of the vasculature that we could discuss with the aid of cardiac output and venous return curves. In stresses that disturb cardiovascular equilibrium, it changes dynamically as volumes redistribute among the organ vasculatures, conduit vessels, and heart. Neither steady-state nor dynamic venous return is properly described as driven by Pms in proportion to the back pressure from Pra.

[1]The use of a single outflow resistance, Rven, ignores the explicit caveat of Guyton et al. that the denominator in their model equation was not the physical resistance of the venous vasculature, but an impedance that combined the resistances and capacitances of all the arterial and venous segments of the vasculature (3).

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Thanks to Loring Rowell for friendship and editorial assistance and for unflagging determination to understand flow and volume dynamics in the cardiovascular system.

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G. L. Brengelmann
University of Washington Department of Physiology and Biophysics
Seattle, Washington
e-mail: brengelm@u.washington.edu

REBUTTAL FROM DR. MAGDER

So close yet so far apart! Dr. Brengelmann finds a "glaring" defect in the balloon model of the circulation and presumably my bathtub analogy (Brengelmann 2006). He argues that the elastic-recoil pressure in the balloon is rapidly dissipated and to "keep Pms constant would require a pump, but then the drive for Fv comes from the pump." I agree with the first part and argued that the heart provides a "restorative" force. However the heart does not "drive" venous return just as the tap filling a tub does not "drive" emptying of the tub. His argument misses Guyton's key point that the "working" cardiac output is determined by interaction of pump *function* (not cardiac output) and return *function* (3) and thus the pump is an integral part of Guyton's analysis. He also fails to deal with the flow that occurs without a pump, even if only transiently and that maximum flow is defined by the ratio of stressed volume (υ) to the time constant of its drainage, which is determined by the product of venous compliance (Cv) and resistance (Rv; Ref. 8).

In the physiological range, Cv is essentially constant so that four variables define the system: flow (Q), υ, Rv [includes the distribution of Q(1)], and right atrial pressure (Pra). A change in one requires a change in at least one of the others (1, 8). The heart only controls Q and Pra. In most of Guyton's experiments, υ and Rv were constant and changes in Pra were related to changes in Q by a changes in cardiac function (or pump in the experiments). In other studies (2, 5), a pump held cardiac output constant, and changes in Pra equivalent required changes in υ or Rv. A physiological example occurs with the rise in Pra and fall in Q with an increase in pleural pressure.

Recruitment of unstressed to stressed volume then increases MSFP and restores Q (6). During aerobic exercise, Q can increase with a constant Pra (7). This requires an increase υ or decreased Rv (4).

In conclusion, steady-state and dynamic VR are properly described by MSFP in proportion to the backpressure. However, steady state *cardiac output* is determined by the interaction of pump and return functions. The heart cannot pump out more than the flow that is determined by the drainage characteristics of the circuit. The heart provides the "restorative force" and, as per Guyton, plays a "permissive" role.

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REBUTTAL FROM DR. BRENGELMANN

Point of agreement: the utility of combining open-loop cardiac and vascular subsystem properties in analyses of cardiovascular stability. For the heart, Pra $\uparrow \rightarrow$ F $\uparrow$; for the vasculature, F $\uparrow \rightarrow$ Pra $\downarrow$. Connected, they form a negative feedback system that stabilizes at the Pra that causes the heart to pump out the F that causes that Pra. Showing this graphically requires plotting one of the relationships with its independent variable on the *y*-axis.

"Waterfall" relevance? Yes, resistance of a vascular segment or Starling resistor increases as it collapses. But, the (Pms−Pra)/Rv concept applies only to the sloped segment of venous return curves, for which intravascular pressures are positive and apparent Rv is constant, i.e., no vessel collapse. About waterfalls: *1*) flow depends only on the flow arriving at the precipice edge; *2*) transport to the lower level is due to gravity; and *3*) they are not enveloped by flexible elastic walls. Why are we talking about them?

Bathtub analogous? In Magder's Fig. 1*A*, (1) we see the right atrium at the level of the water surface and Pra labeled as equal to MSFP (my Pms). But surface level pressure has to be zero, i.e., equal to atmospheric (Patm). Just as the Fig. 1*A* tub cartoon does not correspond to the pressures marked on the graph below it, the hydrostatic relationships are incorrect in the other panels (e.g., pressure at the atrium level would be greater than any in the tub). Correcting all pressures to the same level would reveal the pressure gradient associated with flow, but why pursue this? The (Pms−Pra)/Rv concept is not about blood flowing downhill, and flow in the defining experiments was certainly not driven by gravity. And that faucet? How does it know the flow needed to keep the tub full?

MSFP (Pms) energy source? Quantitatively, the elastic work that moves blood out of a compartment equals the integral of instantaneous pressure times compartment volume decrement dV. Magder's compartment at Pms, kept at constant volume for steady states, has no dV. No dV, no energy release.

To Magder's "what makes the blood go around?" (1, first sentence), I reply *not elastic energy from a compartment at Pms*; but the work manifested in the integral of P times dV for the ventricles (ignoring for the purposes of the present argument the energy input by vessel compression and expansion due to activity of skeletal and respiratory muscles).

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The following letters are in response to the Point:Counterpoint series "The classical Guyton view that mean systemic pressure, right atrial pressure, and venous resistance govern venous return is/is not correct" that appears in this issue.

To the Editor: I believe Dr. Brengelmann's (1) criticism of the Guyton model of the interaction between the circulation and the heart in controlling cardiac output (2) is wrong as validated by clinical observation. As initially described by Mitzner and Goldberg (3) using a right heart bypass preparation, cardiac output cannot be increased by increasing the pump speed in patients undergoing cardiopulmonary bypass unless reservoir volume or fluid resuscitation simultaneously occur. Although the "bathtub" analogy of Dr. Magder (4) is overly simplistic in lumping one reservoir and a single outflow circuit, it correctly models the role that cardiac function plays in determining cardiac output. We previously showed that the cyclic change in right atrial pressure induced by positive pressure ventilation alters pulmonary flow and their relation approximates an instantaneous venous return curve (5). Furthermore, venous return physiology explains the development of acute cardiogenic pulmonary edema. If the only thing that happened with myocardial ischemia was decreased contractility, then cardiac output would decrease but filling pressure would not rise greatly because its upstream mean systemic pressure is only ~10 mmHg. What causes the acute increase in filling pressure is the associated increased sympathetic tone decreasing vascular unstressed volume, increasing mean systemic pressure for the same blood volume. This also explains why sympathetolytic agents rapidly improve cardiovascular status (6). Thus the Guyton model of the control of the circulation is strongly supported by real-life examples and explains the pathophysiology of disease and can be used to define appropriate therapy.

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Michael R. Pinsky
University of Pittsburgh
e-mail: pinskymr@ccm.upmc.edu

To the Editor: The systemic circulation can be viewed as an elastic compartment analogous to the lungs. The respiratory physiologist has no problem in understanding the role of elastic recoil pressure as a determinant of expiratory flow, because expiration typically occurs by the passive recoil of the elastic elements of the lung. It may be difficult to visualize expiratory pressure and flow relations under isovolume conditions, because air cannot move out of the lungs at constant lung volume. It was only with the construction of expiratory pressure-flow relations under isovolume conditions (not a simple exercise!; Refs. 2, 3) that expiratory flow limitation was understood, and this resulted in an appreciation of the role of elastic recoil pressure as a major determinant of maximum expiratory flow (4, 5).

The isovolume venous return curve presents the opposite dilemma to the circulatory physiologist. How can the emptying of a balloon have any relevance in an isovolume system? Thus Brengelmann's inference that "the balloon model has a glaring defect . . . because outflow would remove volume from the elastic compartment, prohibiting the isovolume conditions of the venous return curve" (1). The conceptual necessity of continuous replacement of the draining volume of the systemic circulation obscures the role of the simultaneous mechanics of emptying (elastic recoil and resistance to venous return) that determines the maximum attainable cardiac output. The circulatory or respiratory pressure-flow isovolume curves, remarkably similar to each other, arise from the same mechanical principles and clearly reveal how flow may become independent of the activity of the pump.

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Solbert Permutt
The Johns Hopkins University

To the Editor: Magder (5) depicted arterial inflow as a tap in a bathtub. However, in a circulatory system, there are many bathtubs. Flowing from the heart to any bathtub, blood has to travel a long journey by passing through tubes of decreasing cross sections. How to supply all bathtubs with the appropriate amount of blood becomes an important task for the heart. The heart is designed to provide enough power for blood transportation in an efficient way via pulsatile pumping.

Pulsatile pumping makes blood propagate as a wave not as a direct flow. It is the same strategy as using AC transmission line to replace DC current for long-distance electric power delivery. Pressure gradients and flow in the vasculature develop hand in hand as a consequence of pumping (1). Movement of the blood in artery is governed by a pressure wave equation (3) not by the Poiseuille's Law. In other words, left ventricular output is delivered through pressure wave, offering all bathtubs the sufficient blood and energy source for venous return. Pulse pressure is transmitted deeper into the microcirculation (2). Without a pulsatile pump, only bathtubs near the heart may get enough blood.

Heart rate control is an important regulation for proper blood supply. Frequency-matching rules (4) are the matching relations between heart rate and the natural frequencies of arterial systems or organs. Fulfilling these rules enhances the efficiency of power transportation, and these rules can be used to explain how heart rate and total blood flow change during exercise.

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Yuh-Ying Lin Wang
Wei-Kung Wang
Department of Physics
National Taiwan Normal University

To the Editor: Hydraulic resistance is customarily defined as a pressure drop divided by flow (when gravitational and temperature gradients can be ignored). The entire systemic resistance, (MAP−RAP)/CO, can be split into its serial components (e.g., Rprecap), each defined as the appropriate ΔP divided by CO. Guyton's definition of "the resistance to venous return" [Rvr = (MSFP−RAP)/VR] is unconventional because the driving pressure does not exist while blood is flowing and because Rvr cannot be identified with any particular series component of the circuit. MSFP should not be confused with the average pressure in the system or any pressure in the system while blood is flowing. Rvr is not specifically the flow resistance through the venous system. Guyton himself pointed out in his textbook that about one-third of Rvr was in arterioles and small arteries.

The concept of Rvr arose from "venous return curves" where flow increases as RAP decreases below MSFP. The obvious explanation for this relationship is that, in these experiments, the decrease in RAP and increase in VR were both caused by an experimental increase in CO, as discussed by Brengelmann.

The argument that elastic recoil force in vessel walls provides the driving force for VR (aka CO) is specious. Vessel wall tension and blood flow are both maintained by the left ventricle.

As a teacher of cardiovascular physiology, I have always avoided the fussy and misleading concept of Rvr and the notion that MSFP is the driving force. Neither concept is useful.

R. David Baker
UTMB

To the Editor: A careful reading of Guyton's papers (2, 3) related to the mean systemic pressure (Pms) shows that the junction of his "cardiac function curve" with his "venous return curve" at a specific right atrial pressure (Pra; Ref. 3) is valid only at equilibrium conditions. It was not designed to provide the dynamic characteristic of the cardiovascular system during disturbances. Furthermore, a simple "venous resistance" (Rsv) to flow is not part of Guyton's concept. It is the "resistance to venous return," which is a complex combination of systemic resistances and compliances (2). Neither author seems to realize that a simple Rsv must be associated with a systemic peripheral venous pressure (Psv), which cannot currently be measured but can only be assumed to be similar in magnitude to the Pms. Furthermore, the Pms is a fixed pressure at a given total systemic stressed volume and total systemic compliance. The Pms is not changed by a change in cardiac output or venous return. A decrease in flow from the arteries will lead to a passive decrease in systemic venous stressed volume (because inflow is less than outflow) and a decreased Psv (because the volume is less) at a constant Pra. An increase in right ventricular function will lead to a decreased Pra and then an increase in venous return. These changes will lead to redistributions of blood volume based on the integral of inflow minus outflow for each compartment. (The principal of mass balance, see Ref. 6).

In retrospect, I wish that I had been more explicit (5).

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Carl Rothe
Indiana University School of Medicine

To the Editor: This is a most curious controversy (1, 2), seemingly so 20th Century. In fact, it is not clear what the controversy really is, because no sane person can argue with the fact that venous return must equal cardiac output in the steady state. So, if we agree to deal exclusively with the steady state, then the only question is what are the hemodynamic relations that exist in the peripheral circulation? In this regard, Dr. Brengelmann seems to have misinterpreted the question. Of course there is no steady-state flow if the heart is dead, but because even the most powerful heart cannot generate blood, in the steady state the heart's ability to pump blood is limited to what comes back to it. The blood flow returning to the heart is driven by the difference between the elastic recoil pressure of the peripheral circulation and the pressure at the input to the heart, i.e., the right atrium. This is fact—hardly something to be debated on expensive journal pages. What can be discussed is how best

to model this peripheral circulation, and given the highly nonlinear pressure-volume properties of the peripheral vasculature with its complex parallel vascular pathways, this is still not entirely understood. Nevertheless, the bottom line is the same as it was well before Guyton (or anyone else) even thought about it, that steady-state flow back to the heart is always determined by a mean pressure gradient divided by an effective equivalent resistance, properly designated as the resistance to venous return.

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Wayne Mitzner
Johns Hopkins University

The following letter is in response to the Point:Counterpoint "Active venoconstriction is/is not important in maintaining or raising end-diastolic volume and stroke volume during exercise and orthostasis" that appeared in the October issue.

To the Editor: Hainsworth and Drinkhill (4) argue against the importance of active venoconstriction in raising right atrial pressure (RAP) during exercise based in part on a low reserve of blood volume that can be mobilized by baroreflex-induced increases in sympathetic activity. Because the arterial baroreflex is largely a resistance-raising reflex and not a flow-raising reflex (1, 2), the low reserve is perhaps not surprising. In sharp contrast, the pressor response to muscle ischemia (termed the muscle chemoreflex or muscle metaboreflex) during dynamic exercise is produced almost entirely by an increase in cardiac output, the maintenance of which likely requires substantial venoconstriction (5, 6). Accordingly, we have demonstrated that the muscle chemoreflex is threefold more potent in raising right atrial pressure (5) than are the arterial baroreflexes (1). Moreover, when arterial pressure is maintained constant by ventricular pacing, strong activation of the muscle chemoreflex can reflexly raise RAP by 8 mmHg (5), a substantial fraction of which is likely due to extrasplenic venoconstriction (3). Therefore, it appears that the reserve capacity for central blood volume mobilization in conscious dogs during exercise is much greater than suggested by Hainsworth and Drinkhill (4). However, the extent to which the muscle chemoreflex is active during normal exercise remains a pressing issue.

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Don D. Sheriff
Department of Exercise Science
The University of Iowa
Iowa City, Iowa

Robert A. Augustyniak[1]
Donal S. O'Leary[2]
[1]Departments of Medicine and Physiology
[2]Department of Physiology
Wayne State University School of Medicine
Detroit, Michigan
e-mail: don-sheriff@uiowa.edu

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Last Word: Point:Counterpoint author responds to commentaries on "The classical Guyton view that mean systemic pressure, right atrial pressure, and venous resistance govern venous return is/is not correct"

To the Editor: In my Counterpoint (2), space did not permit mention of the dynamics accompanying each heartbeat that Lin Wang (4) focuses on. Of course, diastolic flow is driven by elastic energy stored from previous systoles as is any discrepancy between cardiac output and venous return. But in the (Pms−Pra)/Rv concept, variables are time averaged over multiple heartbeats; this was certainly so in the experiments that introduced us to venous return curves (e.g., Ref. 3). Measurements were made during steady states—brief ones, but steady in the sense that time-averaged flows, volumes, and pressures were not changing ["steady state" does not mean zero flow, as Mitzner (4) seems to suggest]. The energy dissipated against vascular resistance by steady flow passing through the constant volume vascular compartments was supplied by the heart (and pump), not by shrinking elastic vessels. The experiments from which the (Pms−Pra)/Rv concept arose (3) were not about pulsatile dynamics nor venous return:cardiac output imbalances.

Rothe (5) mentions his model. It represents the peripheral vasculature as two resistors in series with two capacitors connected at the nodes. I regret that he represents the venous system with a single resistor (Rsv) and capacitance, thus not showing the redistribution of volume within the venous system that accompanies flow change (and I hope he will expand the model to represent at least 2 parallel organ vasculatures). Nonetheless, like the model I used (1), Rothe's predicts an inverse flow:Pra relationship. By separating his peripheral vascular components from the heart at the upstream end of the arterial resistor and maintaining total volume constant, one can vary flow and generate the inverse relationship with Pra familiar from venous return curves. One would not interpret this as indicating that venous return is driven from a compartment at fixed Pms acting as the pressure head on the upstream end of Rv, especially because the apparent Rv does not equal his Rsv. Also, his model of the vasculature will not yield the segment of a venous return curve where flow is constant despite progressively reduced Pra. To do so would require nonlinear resistance elements with properties similar to collapsible blood vessels.

Permutt (4) focuses on this flow limitation phenomenon, undeniably of fundamental importance. I would defer to him for discussion of the far-reaching significance of the finding revealed in the original studies of Guyton et al. (3) that central venous pressures fall toward zero when high levels of flow redistribute volume upstream. However, flow limitation by nonlinear vessel properties is not what (Pms−Pra)/Rv describes; it is about the apparent linear increase in flow with progressive reduction in Pra. That is what led to the misconcept that fixed Pms drives venous return. Although Mitzner may think it trivial to debate what (Pms−Pra)/Rv means, even in this 21st Century it is still associated with confusion and absurdities such as bathtub models for the vasculature and flow driven by elastic chambers at constant volume. I have no intention of throwing out the baby, only the bathtub.

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G. L. Brengelmann
Department of Physiology and Biophysics
University of Washington
Seattle, Washington
e-mail: brengelm@u.washington.edu

Last Word: Point:Counterpoint author responds to "The classical Guyton view that mean systemic pressure, right atrial pressure, and venous resistance govern venous return is/is not correct.

To the Editor: Mitzner (4) considers the concept so obvious that he asks why we even needed to have this debate. I agree! The key point is that the elastic properties of the system impose limits on the capacity of the system, and the heart can never surpass these.

Permutt's (4) analysis is based on an elastic compartment analogous to lungs. He emphasizes the crucial but difficult to comprehend concept of the isovolumetric pressure-flow relationship in a system of elastic and collapsible tubes that can create flow limitation. Personally, I never understood cardiovascular physiology until I was presented with this comparison to respiratory physiology and I recommend readers who are unfamiliar with it to consult J. F. Green's monograph (2) and the paper by Permutt and Caldini (3).

Green (2) suggests the analogy of a toilet instead of a bathtub. Besides being less aesthetically pleasing, it misses the key point of isovolumetric conditions. Perhaps further consideration of the bathtub model may help emphasize the importance of the isovolume condition of the elastic region. When the tub is filled to the top, increasing the force or flow from the tap does not affect flow from the drain because the inflow cannot raise the height of the water in the tub.

Baker and Rothe (4) raise the issues of multiple bathtubs or varying positions of the MSFP and the localization of venous resistance. Whereas these comments are valid, a close approximation can be made by a lumped parameter model that deals with the weighted effects of the different compliant regions and what Mitzner (4) appropriately calls the "effective equivalent resistance." The formal mathematical analysis for these was presented by Permutt and Caldini (3). The "fussy" concept of MSFP is essential for understanding the limits of the system. This debate is about steady-state conditions, although the concepts still apply in dynamic situations. Consider, for example, the model of Burkoff and Tyberg (1).

Wang's (4) comments refer to pulsatile flow. Clearly the heart is the source of these pulsations, but this must not be confused with the total flow through the system. Humans have normal cardiac outputs without pulsatile flow on a daily basis in the cardiac surgery suite. However, the importance of the volume of the circuit is also very obvious in these patients when flow limitation occurs; pump flow then can only be increased by adding volume and thus increasing the elastic recoil pressure.

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S. Magder
Division of Critical Care Medicine
McGill University Health Centre
Montreal, Quebec, Canada
e-mail: sheldon.magder@muhc.mcgil.ca