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 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) 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 the venous return of 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
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 $R_v \times C_v$.

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 drained 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.

REFERENCES
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 led 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.

Nor was Fv set by adjusting Pra. It is not generally recognized that the Starling resistor circuit was the control element in a closed feedback loop and that its variable resistance, not Pra back pressure, caused Fv changes. What Guyton et al. varied as an independent variable was resistor height, not Pra.

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;