A Postscript to Circulation of the Blood: Men and Ideas

Richard L. Riley, M.D.

SUMMARY  Since 1964, when Fishman and Richards published Circulation of the Blood: Men and Ideas, Guyton’s model of the circulation, in which mean circulatory pressure serves as the upstream pressure for venous return, has been extended, and the concept of vascular smooth muscle tone acting like the pressure surrounding a Starling resistor has been postulated. According to this scheme, the positive zero flow intercepts of rapidly determined arterial pressure-flow curves are the effective downstream pressures for arterial flow to different tissues. The arterioles, like Starling resistors, determine the downstream pressures and are followed by abrupt pressure drops, or “waterfalls.” Capillary pressures are closely linked to those of the venules into which they flow. Capillary-venular pressures are the upstream pressures for venous return. In exercising muscles, reduced arteriolar tone lowers arteriolar pressure and increases arterial flow. This, in turn, raises capillary-venular pressure and increases venous flow. The arteriolar-capillary waterfall is decreased or eliminated. Total blood flow is increased by diversion of blood from tissues with slow venous drainage to muscles with fast venous drainage (low resistance × compliance). The heart pumps away the increased venous return by shifting to a new ventricular function curve.

In the early days of World War II, I worked under Dickinson Richards and Andre Cournand on the Shock Team at Bellevue Hospital in New York. The centerpiece of this comprehensive study of traumatic shock was the newly developed technique of human cardiac catheterization. These studies set off an avalanche of catheterization applications, first at Bellevue and later all over the world. The extraordinary skill and wisdom shown by Drs. Richards and Cournand in guiding cardiac catheterization through the early years are well known.

Dickinson Richards liked to stay behind the scenes, quietly examining data, making policy decisions and reassuring worried administrators. He was, however, very much on the spot at any time of the day or night when studies were under way. Modern medicine and clinical investigation are much in his debt.

Two essential features of the control of blood flow were only vaguely understood at the time of the Bellevue studies: The fact that the Frank-Starling ventricular function curve is actually a family of curves had not yet been shown by Stanley Sarnoff, and the peripheral factors controlling blood flow had not yet been clarified by Arthur Guyton. When Fishman and Richards published Circulation of the Blood: Men and Ideas in 1964, Sarnoff’s contribution was included, but Guyton’s concepts, still very controversial, did not appear. I have called my lecture “A Postscript” to the book edited by Fishman and Richards both to do justice to Guyton and to pull together other ideas that have evolved since the publication of that beautiful and scholarly book.

Blood Flow vs Air Flow

As a respiratory physiologist it was easy to be one of Guyton’s early supporters. He made blood vessels seem like lungs. My discussion of blood flow begins with an analogy to air flow.

Consider a model in which both the lung-airway system and the peripheral vascular system are represented as elastic balloons that are filled and emptied through collapsible tubes (fig. 1). The airways have one tube for bidirectional flow, and the blood vessels have two tubes for arterial and venous flow. The elastic elements are lumped in the alveoli and the small veins, a liberty that does but slight injustice to the facts. The lungs are held open from without by the chest wall, while the vascular system is held open from within by the blood. The pump that further distends the compliant alveoli in inspiration is predominantly the diaphragm, and the pump that ejects blood through the arteries and into the compliant small veins is the heart. The force that empties the lungs in expiration is the elasticity of the lungs and chest wall; in the absence of skeletal muscle activity, the force that returns the blood to the heart is the elasticity of the capacitance vessels. Because the airways collapse, the muscles of respiration cannot appreciably speed up expiration, and because the veins collapse on entering the thorax, the heart cannot significantly speed up venous return.

Dr. Riley is Professor Emeritus, Departments of Medicine and Environmental Health Sciences, The Johns Hopkins University, Baltimore, Maryland.

Presented at the 54th Scientific Sessions of the American Heart Association, Dallas, Texas, November 16, 1981.

Address for correspondence: Richard L. Riley, Petersham, Massachusetts 01366.

Received January 27, 1982; accepted March 29, 1982.

Circulation 66, No. 4, 1982.
Airways collapse when intrapleural pressure is positive, as in forced expiration, and veins collapse when intrapleural pressure is negative. These are variations on Guyton’s mean circulatory pressure theme and on Holt’s venous collapse theme. Any doubts concerning the surprising fact that the heart alone cannot greatly increase cardiac output were put to rest by Permutt and Caldini. They replaced the heart of an anesthetized dog with a roller pump and found that turning up the pump collapsed the great veins but caused little increase in blood flow.

**Arterial Flow**

In 1963, Permutt and Riley suggested that vascular smooth muscle could act like the surrounding pressure in a Starling resistor and that arteriolar tone might, under appropriate circumstances, determine the effective downstream pressure for arterial flow. The fact that arterial pressure-flow curves have a positive intercept at zero flow has been known since Whitaker and Winton’s paper was published in 1933. More recently, arterial pressure-flow curves determined during a single prolonged diastole have carried the curves to zero flow before reflex changes in vascular tone could occur. Studies by Ehrlich et al., Jackman and Green, Bellamy, Downey and Kirk, Klocke et al., and others have provided pressure-flow curves for many different vascular beds, including the coronary vessels. These pressure-flow curves are remarkably straight (fig. 2). The zero-flow intercepts for the different vascular beds occur at widely different pressures, being very high, even above aortic diastolic pressure, in the femoral artery and as low as 20 mm Hg in the renal artery (fig. 3). There can no longer be reasonable doubt that the slope of the rapidly determined arterial pressure-flow curve is inversely related to arterial resistance and that the zero-flow intercept represents the effective downstream pressure for arterial flow. This pressure is a function either of arteriolar tone or of the pressure in the venous capacitance vessels.

**Arteriolar-Capillary Waterfall**

If arteriolar tone is equivalent to the pressure surrounding a Starling resistor, when arteriolar pressure exceeds capillary pressure, there is every reason to expect an abrupt pressure drop, or vascular waterfall, to use the term coined by Permutt. In the peripheral circulation, the pressure must drop abruptly from the arteriolar value to the value at the upstream end of the capillaries. If one takes an upstream capillary pressure of 35 mm Hg, as given in many texts, there remains a sizable gap between arteriolar and capillary pressures.

![Figure 1: Model showing similarities between breathing and blood flow. Narrowed segments of airways and vessels represent partial collapse as in a Starling resistor. H = heart; a = arteries; v = veins; ++ = positive intrathoracic pressure; -- = negative intrathoracic pressure.](image1)

![Figure 2: Pressure-flow graph obtained during cardiac arrest, sampled in 50-msec intervals. Q = artery flow; Pao = pressure in abdominal aorta. X indicates the same value for more than one interval. From Ehrlich et al. Reproduced with permission of the American Heart Association.](image2)

![Figure 3: Arterial pressure (P)-flow (Q) curves from several vascular beds. The femoral artery before a 30-second occlusion (extreme right) could not be studied accurately. Adapted from Ehrlich et al. 1981, with permission from the American Heart Association.](image3)
in many vascular beds. This gap is precisely where one would expect a vascular waterfall.

**Venous Flow**

The venous side of the peripheral circulation was studied in dogs by Caldini et al. in 1974. These authors used a right-heart bypass preparation and observed the characteristics of venous drainage after a step decrease in right atrial pressure. The data could not be explained by assuming a simple elastic system, but were satisfactorily accounted for by postulating two vascular compartments with slow and fast time constants of drainage (fig. 4). I have extended the analysis of Caldini et al. to calculate upstream pressures for venous return for both slow and fast compartments. Guyton-type venous return curves for both compartments were drawn by connecting average upstream pressures at zero flow with average flows at zero downstream pressure (fig. 5). The upstream pressure for venous return was 7.2 mm Hg for the fast compartment and 15.6 mm Hg for the slow compartment. The fast compartment had a little less flow than the slow compartment. Although no one has repeated exactly the experiments of Caldini et al., Green and Mitzner and Goldberg confirmed the basic fact that different vascular beds have different time constants of venous drainage. We are not concerned here with differences in upstream pressure found by different investigators.

With the advent of multicompartmental models, mean systemic pressure can no longer be considered the upstream pressure for venous return, as the pressures in the capacitance vessels of different compartments usually differ. These pressures still depend, as Guyton saw, on the elastic properties of the capacitance vessels, and their pressures still provide the force that drives the blood back to the heart.

**Schematic of the Systemic Circulation**

Figure 6 has the same format as the familiar diagram appearing in most texts and shows the pressures in different parts of the systemic circulation. The arteriolar pressures, 60 and 40 mm Hg, are in the range of zero-flow intercepts for arterial pressure-flow curves and are illustrative values not based on specific data. The upstream pressures for venous return from the slow and fast compartments are from figure 5. The gradients between aortic and arteriolar pressures are the driving pressures for arterial flow. The gradients between venular and vena caval pressure are the driving pressures for venous return. The differences between arteriolar and venular pressures, shown by vertical dots, are attributed to vascular waterfalls. The bigger waterfall exists when arterial and venous driving pressures are smaller, that is, when blood flow is throttled down by constricted arterioles, as in the fast compartment in figure 6. The arterial and venous driving pressures are larger and the waterfall smaller in the slow compartment. When the demand for blood flow is greatest, as in strenuously exercising muscles, the waterfall may be eliminated completely, providing maximal driving pressures for arterial and venous flow, as shown by the curve on the right in figure 6.

**Capillary Pressure and Fluid Exchange**

Where in this scheme of things is capillary pressure? Capillary and venular pressures are, for practical purposes, the same. Calculations suggested by Mitzner (personal communication) indicate that the pressure...
The increased total capacitance vessels of the slow compartment. More important are venous return curves for slow (S) and fast (F) compartments after administration of epinephrine (EPI) derived from data of Caldini et al. Broken lines show control findings before epinephrine and are identical to those in figure 5. Q = flow; P = pressure.

**Control of Blood Flow**

If the heart cannot appreciably speed up venous return because the veins collapse on entering the thorax, by what mechanism are venous return and hence cardiac output increased? If the discussion is limited to the experimental animal in the horizontal posture with inactive skeletal muscles, then according to Guyton's original model the options were limited: Mean circulatory pressure could increase and resistance to venous return could decrease. The two-compartment model added a third important option: More of the arterial flow can be diverted from the slow compartment to the fast compartment. More blood in the capacitance vessels of the fast compartment increases upstream pressure for venous return from this compartment, and flow is greatly increased. The corresponding reduction in blood volume in the capacitance vessels of the slow compartment reduces flow in that compartment only slightly. The increased total venous return is pumped into the arterial system, and right atrial pressure does not increase, as the heart shifts to a new ventricular function curve.
Arterial and Venous Pressure-Flow Curves: Rest and Exercise

Figure 8 shows arterial and venous pressure-flow curves after administration of epinephrine. For simplicity, the curves are for total flow in which fast and slow compartments are combined. The broken line for the arterial curve indicates that it is an estimate, as it was not determined by Caldini et al. The horizontal dots between the downstream pressure for arterial flow and the upstream pressure for venous flow represent the vascular waterfall. For convenience, the waterfall is shown along the zero-flow axis even though it is a dynamic event that occurs only during flow. The horizontal line marked EPI shows the unimpeded flow in all parts of the system. The beauty of this graph is the simultaneous demonstration of arterial and venous pressure-flow curves and the arteriolar-capillary waterfall.

Muscular contraction increases tissue pressure and squeezes the capacitance vessels within the muscle. This increases the upstream pressure for venous outflow, empties the capacitance vessels, and increases venous outflow during a brief contraction. Arterial inflow to the muscle, which is impeded by high tissue pressure, is smaller during the contraction phase. The filling and emptying of the capacitance vessels make possible this asynchrony between inflow and outflow in a rhythmically contracting muscle.

Figure 9 shows coronary arterial pressure-flow curves for systole and diastole adapted from Bromberger et al. (unpublished data presented at XXVIII International Congress of Physiological Sciences, Budapest, 1980). I have added assumed venous outflow curves, shown by broken lines. The increased tissue pressure during systole displaces to the right the zero-flow intercepts for both arterial and venous flow. The reciprocal changes in arterial inflow and venous outflow during systole and diastole are shown by the peak flows of the respective curves. Arterial inflow is about 40 ml/100 g tissue/min in systole and 125 ml/100 g tissue/min in diastole, whereas venous outflow is about 175 ml/100 g tissue/min in systole and 35 ml/100 g tissue/min in diastole. Total flow for the cardiac cycle is the same for inflow and outflow, as indicated by the large black dots (somewhat closer to diastolic flow than systolic because of the longer duration of diastole).

A hard-working muscle like the heart increases its blood flow by relaxing arteriolar tone, thereby reducing the arterial zero-flow intercept (20 mm Hg in diastole for the example in figure 9). The resulting high arterial inflow in diastole (125 ml/100 g tissue/min) distends the capacitance vessels, thereby raising the upstream pressure for venous outflow and reducing or eliminating the arteriolar-capillary waterfall (fig. 6, right-hand curve). In figure 9, the upstream pressure for venous outflow is assumed to be the same as the downstream pressure for aterial inflow (20 mm Hg in diastole), implying that the waterfall has been eliminated. This assumption is made, in part, because it seems unlikely that capillary pressure would be less than 20 mm Hg, as would be the case if an arteriolar-capillary waterfall existed. Further, an arteriolar-capillary waterfall subtracts from the total driving pressure available for arterial and venous flow, and it seems unlikely that a muscle would be designed to restrict its blood flow when actively working. These relationships remain the same in systole, though displaced to the right by almost 70 mm Hg by the increased tissue pressure. Arterial and venous resistances (slopes of the curves in figure 9) change little throughout the cardiac cycle.

Figure 8. Arterial and venous pressure (P)-flow (Q) curves after administration of epinephrine (EPI). Slow and fast compartments are combined to give total flow. Broken line indicates that arterial curve (a) was not experimentally determined. Dots along horizontal axis indicate vascular waterfall. Flow in all parts of unimpeded system indicated by horizontal line marked EPI.

Figure 9. Coronary arterial (a) and venous (v) pressure (P)-flow (Q) curves in systole and diastole. Broken lines indicate assumed venous outflow curves. Large dots indicate arterial and venous flow for complete cardiac cycle. Absence of waterfall implies low arteriolar tone for high perfusion. Q_LCA = left coronary artery flow; H = heart; SYST = systole; DIAST = diastole. Arterial curves after Bromberger-Barnea, Wise and Taylor, 1980, with permission of the authors.
I now view the arteriolar-capillary waterfall as existing in tissues, such as resting muscle, that do not need maximal blood flow. This includes most tissues most of the time. In a hard-working muscle like the heart, the waterfall is reduced or eliminated, and my guess is that the same applies to skeletal muscles during strenuous exercise.

In summary, breathing and blood flow have comparable active phases — inspiration and cardiac ejection — and comparable passive phases — expiration and venous return. The tubes in both systems are collapsible and, under appropriate conditions, act like Starling resistors.

Arterial pressure-flow curves have a positive pressure intercept at zero flow. This arterial downstream pressure is usually determined by arteriolar tone and differs widely in different tissues. In hard-working tissues that need maximal blood flow, the arterial downstream pressure may be the pressure in the venous capacitance vessels.

Venous pressure-flow curves have upstream pressures that represent the pressures in the capacitance vessels. These pressures differ widely between compartments with fast and slow drainage but are usually below arteriolar pressure. When present, the pressure gap between arterioles and venules is accounted for by a vascular waterfall.

Capillary pressure is believed to be determined by the pressure in the capacitance vessels into which capillaries drain. This assures that capillary fluid shifts keep blood volume adjusted to the size and compliance of the vascular bed.

Blood flow is increased during exercise by diversion of blood from slow to fast time constant beds. Relaxation of arteriolar tone in hard-working muscles reduces or eliminates the arteriolar-capillary waterfall that is present at rest. The heart pumps away the increased venous return without an increase in right atrial pressure by shifting to a new ventricular function curve.

References
1. Sarnoff SJ: Myocardial contractility as described by ventricular function curves; observations on Starling’s law of the heart. Physiol Rev 35: 107, 1955
A postscript to Circulation of the blood: men and ideas.
R L Riley

Circulation. 1982;66:683-688
doi: 10.1161/01.CIR.66.4.683
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1982 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on
the World Wide Web at:
http://circ.ahajournals.org/content/66/4/683

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/