

## Venous Function and Central Venous Pressure

### A Physiologic Story

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The veins contain approximately 70% of total blood volume and are 30 times more compliant than arteries; therefore, changes in blood volume within the veins are associated with relatively small changes in venous pressure. The terms *venous capacity*, *compliance*, and *stressed and unstressed volumes* are defined. Decreases in flow into a vein are associated with decreases in intravenous pressure and volume, and *vice versa*. Changes in resistance in the small arteries and arterioles may affect venous return in opposite directions; this is explained by a two-compartment model: compliant (mainly splanchnic veins) and noncompliant (nonsplanchnic veins). Effects of intrathoracic and intraabdominal pressures on venous return and central venous pressure as well as the value of central venous pressure as a diagnostic variable are discussed.

IN the era of genetic revolution and exciting discoveries in molecular mechanisms of diseases, the systems' physiology is often forgotten and poorly understood by many, including anesthesiologists. This review intends to cover one of many gaps in the understanding of cardiovascular physiology. The main goal of this article is to describe the functions of the venous system as an important part of the overall cardiovascular physiology. Understanding of these functions would help to prevent many mistakes in the interpretation of one or another variable, particularly values of central venous pressure (CVP), in clinical settings.

Schematically we can look at the cardiovascular system as a heart and a circuit. This article is focused on one part of the circuit, namely the venous system. The function of the heart and the arterial system will be mentioned only in light of their effects on the venous system and the effects of the venous system on the function of the heart. Moreover, the focus of this article is on the gross phys-

ologic relation within the venous system rather than on molecular and biochemical mechanisms of smooth muscle contraction and relaxation of the venous walls. Finally, the article will address the question of usefulness (or lack of it) of the CVP as a clinical guide for physiologic diagnoses and therapeutic interventions.

### Function of the Venous System

The main functions of the venous system are to return blood to the heart from the periphery and to serve as a capacitance to maintain filling of the heart. Veins contain approximately 70% of total blood volume compared with 18% in arteries and only 3% in terminal arteries and arterioles; veins are 30 times more compliant than the arteries.<sup>1,2</sup> The compliance of the arteries, being much lower than compliance of the veins, may increase under certain conditions, *e.g.*, arterial compliance significantly increases during pregnancy<sup>3</sup> and during certain pharmacologic interventions such as nitroglycerin administration.<sup>4,5</sup> The splanchnic system receives approximately 25% of cardiac output (CO) and contains approximately 20% of total blood volume. Because of high compliance of the veins, changes in blood volume are associated with relatively small changes in venous transmural pressure.<sup>2</sup> Veins are the most compliant vasculature in the human body and are easily able to accommodate changes in the blood volume. Therefore, they are called *capacitance vessels* and serve as a reservoir of blood that easily and immediately changes volume in it to maintain filling pressure in the right heart. Splanchnic and cutaneous veins are the most compliant and represent the largest blood volume reservoirs in the human body. Veins of the extremities are less compliant than splanchnic veins, and therefore, their role as blood volume reservoir is relatively minimal. Splanchnic and cutaneous veins have a high population of  $\alpha_1$ - and  $\alpha_2$ -adrenergic receptors and therefore are highly sensitive to adrenergic stimulation, contrary to skeletal muscle veins, which have relatively insignificant sympathetic innervation.<sup>6</sup> This pattern of innervation of the veins and the fact that cutaneous circulation is controlled mainly by the temperature suggest that venoconstriction and mobilization of blood volume is mainly limited to the splanchnic veins.<sup>7,8</sup>

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## Definitions and Basic Concepts

### Venous Capacity and Compliance

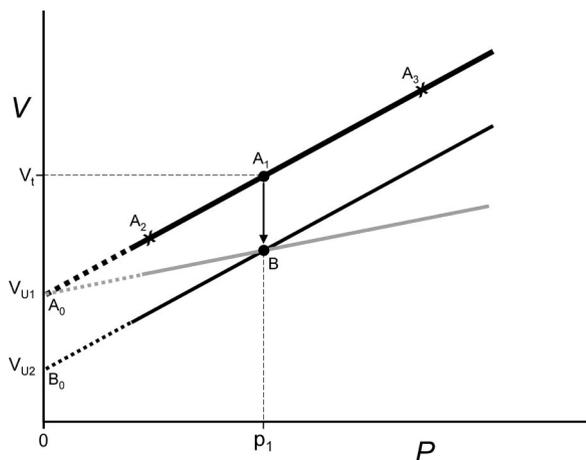
There is some confusion in the literature regarding the relevant terminology. The definitions described in this article are used by the majority of authors and clearly summarized by the authority in the field.<sup>1,9</sup>

*Venous capacity* is a blood volume contained in a vein at a specific distending pressure.<sup>6,9-11</sup>

*Venous compliance* is a change in volume ( $\Delta V$ ) of blood within a vein (or venous system) associated with a change in intravenous distending pressure ( $\Delta P$ ).

$$\text{Venous Compliance} = \Delta V / \Delta P. \quad (1)$$

Therefore, capacity is a point of volume at a certain pressure while compliance is a slope of change in volume associated with a change in pressure. A decrease in volume within a vein (or venous system) can be achieved by a decrease in capacity (position of the curve) or by a change in compliance (slope of the curve) or both (fig. 1). Venoconstrictors,  $\alpha$ -adrenergic agonists, decrease venous capacity without changing compliance.<sup>12</sup>



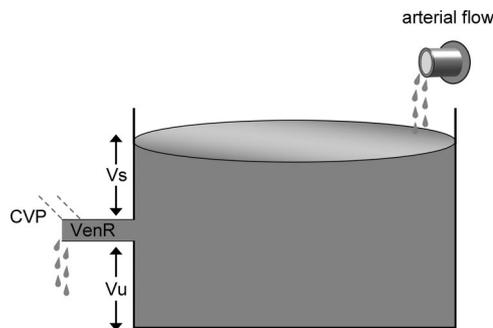
**Fig. 1.** Venous capacity and compliance, stressed and unstressed volumes. Point A1 represents total volume of blood in veins at transmural pressure  $p_1$ . Points A2 and A3 represent change in volume induced by change in pressure within the veins. *Thick black line* represents baseline compliance. Point A<sub>0</sub> is obtained by extrapolation of the thick black line until it crosses the y-axis; this point (A<sub>0</sub>) represents volume of blood at transmural pressure zero, which is unstressed volume ( $V_{u1}$ ). Difference between total volume ( $V_t$ ) and  $V_{u1}$  is stressed volume ( $V_s$ ). When a certain amount of blood is mobilized from the veins, point A1 moves to point B; the veins contain now less blood at the same intramural pressure  $p_1$ . Removal of the volume of blood between points A1 and B may be associated with no change in the slope of the pressure–volume relation (*thin black line parallel to the thick black line*); this means that venous compliance did not change, but capacity did. Point B<sub>0</sub> (*thin black line extrapolated to the y-axis*) represents decreased unstressed volume (from  $V_{u1}$  to  $V_{u2}$ ). However, the pressure–volume relation within the veins might look like the *gray line*. The same amount of blood is mobilized (from point A1 to B), but  $V_u$  did not change: The gray line crossed the y-axis at the same point A<sub>0</sub>; the mobilized blood was recruited by a decrease in compliance rather than from a decrease in  $V_u$ .

It is important to distinguish *intraluminal (intramural) venous pressure*, which is the pressure within a vessel (which can be measured directly *via* an inserted catheter), regardless of the pressure surrounding the vessel. *Transmural pressure* or *distending pressure* refers to a difference between the pressure within the vessel and outside the vessel.

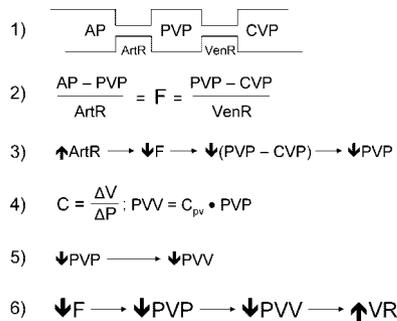
### Stressed and Unstressed Volume

The intersection of the line of compliance with the y-axis reflects an *unstressed volume* ( $V_u$ ; fig. 1), which is a volume of blood in a vein at transmural pressure equal to zero. *Stressed volume* is a volume of blood within a vein under transmural pressure above zero ( $V_s$ ; fig. 1). The sum of stressed (approximately 30% of total volume) and unstressed (approximately 70% of total volume) volumes is the total blood volume within the venous system.

An analog with a tub is helpful to understand the relation between  $V_u$  and  $V_s$ <sup>13-15</sup> (fig. 2). Both volumes are important:  $V_s$  determines mean circulatory filling pressure (MCFP; see Mean Circulatory Filling Pressure section) and directly affects venous return (VR) and CO, whereas  $V_u$  is a reserve of blood that can be mobilized into circulation when needed.



**Fig. 2.** Stressed and unstressed volumes—tub analogy. Water in a tub represents total blood volume. A hole in the wall of the tub between the surface of the water and the bottom of the tub divides total volume into stressed ( $V_s$ ) and unstressed ( $V_u$ ) volumes, above and below the hole, respectively. The water leaves the tub through the hole at a certain rate that depends on the diameter of the hole (which would reflect venous resistance [VenR]), and on the height of the water above the hole, representing  $V_s$ ; the larger the  $V_s$ , the higher the flow through the hole. The water between the hole and the bottom of the tub does not affect the flow of water through the hole; this is the  $V_u$ , a sequestered volume that does not directly participate in the rate of water flow (venous return). With the same amount of water in the tub (total blood volume in the venous system), the relation between  $V_s$  and  $V_u$  can be changed by moving the hole up or down. Moving the hole down represents venoconstriction and increases  $V_s$  (and venous return). The distal end of the tube, attached to the hole in the tub wall, represents central venous pressure (CVP): the higher the distal end, the higher the CVP and the lower the pressure gradient for venous return, and *vice versa*. The inflow tap represents the arterial flow. The hydraulic disconnect between the tap and the tub represents functional disconnection between the two (arterial flow and the venous system) due to high arterial resistance.



**Fig. 3.** Flow–pressure–volume relation in compliant veins. *Line 1* depicts a schema of the terminal and venous part of the circulation. AP, PVP, and CVP represent pressure in arteries, small (peripheral) veins (capillary pressure is incorporated into PVP), and right atrium, respectively. ArtR and VenR represent arterial and venous resistance, respectively. At steady state, the flow (F) through the system must be the same at every point of the schema. Flow is equal to pressure gradient divided by resistance (*line 2*). An increase in ArtR decreases F through the whole system (*line 3*). VenR is much smaller than ArtR and does not change the overall situation within the system. Therefore, because F is decreased, the difference between PVP and CVP must have decreased. To maintain flow through the system, PVP must be higher than CVP. Assuming that CVP remains unchanged (as is almost always the case in normal cardiac function), decreased flow through the system must be associated with a decrease in PVP. Because compliance (C) by definition is a ratio of ΔV to ΔP (equation 1 in the text), the volume within the small veins (PVV) would be equal to compliance in peripheral veins (C<sub>pv</sub>) multiplied by pressure within the veins (PVP, *line 4*). Because an increase in ArtR unavoidably leads to a decrease in PVP (*line 3*) and compliance does not change (fig. 1, black lines), any decrease in PVP must be associated with a decrease in volume of blood within the small veins (PVV, *line 5*). In reality, a decrease in F is associated with an immediate and simultaneous decrease in PVP and PVV. A decrease in PVV leads to a shift of blood volume from the veins to the heart increasing venous return (VR, *line 6*). Therefore, an increase in ArtR, through decreases in PVP and PVV, leads to a temporary increase in venous return (VR, *line 6*). At the moment of decreased arterial flow (inflow), the flow from the veins is not decreased immediately; there is a transient increase in the flow from the veins but then, after the volume is expelled from the veins, the venous outflow decreases and becomes equal to the decreased arterial flow. Therefore, the schema is approximately two steady states, and the transient uncoupling between arterial inflow (decreased) and venous outflow (increased) is short lasting.

*Flow-Pressure-Volume Relation*

This relation is an important homeostatic mechanism in the body,<sup>8,16</sup> (fig. 3). The described relation between flow, pressure, and volume within the veins occurs in very compliant (splanchnic) veins and represents a passive distribution of volume between veins (mainly the splanchnic system) and the heart, which is associated with changes in venous capacity without change in compliance (fig. 1, black lines).

A decrease in flow through the splanchnic arteries, being associated with a decrease in volume in the splanchnic veins and the liver and transfer of this volume into the systemic circulation, plays an important role not only in compensation of hypovolemia but also in compensation of cardiac failure. If CO is decreasing, a simultaneous decrease in flow through splanchnic arteries is

associated with a shift of blood volume from splanchnic veins to the heart recruiting Frank-Starling mechanism (an increase in preload leading to an increase in contractility). Reduction in CO by 27% was associated with 9.2 ml/kg of blood recruitment from the splanchnic system when reflexes were intact.<sup>17</sup> Similar reduction in CO in conditions of ganglioblockade with hexamethonium led to recruitment of blood volume of 6.8 ml/kg. In a 75-kg human, this would mean a shift of blood volume of approximately 700 *versus* 500 ml of blood into systemic circulation with and without reflexes intact, respectively. Therefore, the active constriction of veins would transfer only approximately 25% of total transferred blood.<sup>17</sup> Thus, passive mechanisms due to change in flow followed by change in pressure and volume are more important in maintaining VR and CO than active venoconstricting mechanisms (fig. 3).<sup>8,17</sup>

Passive change in blood volume within the splanchnic system is more important within the intestines, whereas the active constriction of the vasculature is more prominent within the liver.<sup>9,17-19</sup> The distribution of blood flow governs the distribution of blood volume within the body.<sup>17,20</sup> These flow–pressure–volume relations adequately explain many physiologic and clinical conditions. More than 70 yr ago, an enlargement of cardiac dimensions was observed during cross clamping of the thoracic aorta.<sup>21</sup> The authors attributed this to an increased afterload. They also observed that the cross clamping increased “systemic flow” (CO). They attributed (but did not prove) this increase to “blood transference” from the lower to the upper part of the body. Many other studies confirmed these observations.<sup>22</sup> We observed a twofold increase in blood flow through the upper part of the body during aortic cross clamping at the diaphragmatic level.<sup>23-25</sup> Finally, our experiments using whole body scintigraphy with technetium 99m-labeled plasma albumin have demonstrated that aortic cross clamping at the diaphragmatic level is associated with a significant increase in blood volume in the organs and tissues proximal to the level of occlusion.<sup>26</sup> This is a direct unequivocal illustration of the shift of blood volume from the organs distal to the aortic cross clamp (from the compliant splanchnic veins) to the proximal, upper part of the body. Therefore, aortic cross clamping proximal to celiac artery leads to a drastic decrease in splanchnic flow, followed by a decrease in volume within the splanchnic veins and a shift of the volume to the upper part of the body with an increase in VR and CO.<sup>22</sup>

*Mean Circulatory Filling Pressure*

Let us imagine the heart is stopped for a relatively short period of time. Blood will not be flowing from the heart and toward the heart, and pressure will be the same in all parts of the circulatory system. Such a pressure is called *mean circulatory filling pressure*.<sup>27,28</sup>

When the heart starts pumping the blood, pressure within the arterial system is increasing and pushes the blood through the arteries, then through the capillaries into the venous system. The pressure in the small veins becomes higher than in the large veins and right atrium—CVP. Blood flow from the veins into the heart is determined by the gradient between peripheral and central venous pressures. According to Guyton, the main driving force for VR is MCFP, and

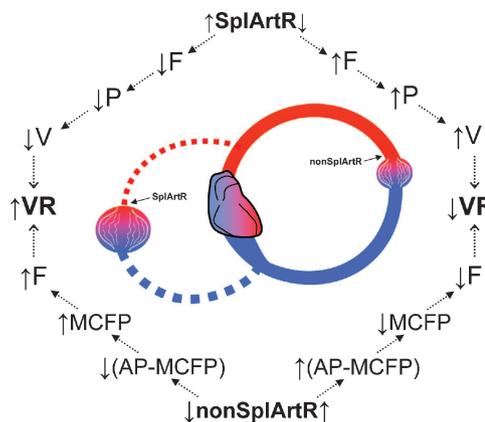
$$VR = (MCFP - CVP)/\text{Venous Resistance.}^\dagger \quad (2)$$

During cardiac arrest, the pressure within the venules and small veins is not changing and remains the same as it was before cardiac arrest. Therefore, this pressure is considered the “pivoting pressure” for the whole circulatory system.<sup>9</sup>

The heart cannot pump more blood into circulation than it receives. Therefore, in physiologic conditions, CO is determined entirely by VR, and VR can be increased only by an increase in MCFP and/or a decrease in CVP because venous resistance is usually not changing much and relatively small. A normal heart itself can increase VR mainly by decreasing CVP, and only to a limited extent by increasing MCFP because of high resistance across arterial (resistance) vessels: The main pressure gradient within the circulatory system occurs at the level of arterial resistance.

The main factor determining the MCFP is  $V_s$ ; others include venomotor tone, the vascular pump, the effects of ventricular contraction and relaxation, and the function of the venous valves and skeletal muscle. In dogs and presumably in humans, MCFP is approximately between 7 and 12 mmHg, whereas CVP is approximately 2–3 mmHg.<sup>15,27–31</sup> Thus, the gradient for VR is somewhere between 5 and 10 mmHg, and therefore, the change in CVP just by a few millimeters of mercury can have considerable effect on VR.<sup>15,32</sup>

An interesting question is why in the normally functioning heart an increase in CVP (e.g., secondary to an infusion of volume) increases CO despite the increased downstream pressure. The tempting answer to this question is because myocardial contractility is increased. But this would not be enough because an increased contractility can increase the ejection fraction and would solve the problem of the heart but would not solve the problem of the circuit. The problem is solved by an increase in MCFP secondary to an increase in  $V_s$ . Because an increase in MCFP is at least equal or usually larger than an increase in CVP, even larger increases in pressure gradient to VR would be achieved at a higher level of both pressures, MCFP and CVP, with subsequent increases in VR and CO.



**Fig. 4.** Two-compartment model. *Inside:* The two circuits represent two compartments; the solid red and blue lines represent the main, basic circuit. Dashed red and blue lines represent arterial and compliant (splanchnic) venous compartments. The compartment with compliant veins is outside of the main circuit. Therefore, changes in arterial or venous resistance in compliant compartment do not directly affect arterial or venous resistance in the main circuit with noncompliant veins. *Thickness of the lines* reflects the amount of flow within the vessels under normal conditions. *The size of the junctions* between arteries and veins reflects the blood volumes contained in the two circuits. *Outside:* Effects of change in arterial resistance feeding compliant (splanchnic) and noncompliant (muscle) veins. SplArtR and NonSplArtR represent arterial resistance in arteries feeding compliant and noncompliant veins, respectively. F, P, and V represent flow, pressure, and volume within the venous vasculature, respectively. AP = arterial pressure; MCFP = mean circulatory filling pressure; VR = venous return. Change in resistance in arteries feeding splanchnic and non-splanchnic vasculature leads to changes in venous return in opposite directions through changes in flows, pressures, and intravenous volumes (see text for explanation).

#### Venous Resistance

Constriction of the veins decreases their capacity and expels blood from them into the systemic circulation. However, venoconstriction may increase venous resistance and subsequently decrease VR and CO. How is the body recruiting the blood volume without an increase in resistance to VR? The constriction of splanchnic veins is not associated with an increase in resistance to VR because the splanchnic system is outside of the mainstream of blood flow to the heart through the caval veins<sup>1,15,33</sup> (fig. 4, inside).

Venous return is increased by an increase in MCFP secondary to an increase in  $V_s$ , which can be achieved by an infusion of additional volume and/or by a decrease in venous capacity by venoconstrictors. The latter decreases  $V_u$  and increases  $V_s$  without change in the elastic properties of the venous wall, *i.e.*, without change in venous compliance (fig. 1). In the analog with the tub, the outlet hole in the tub is moved down by venoconstriction: increasing the volume above the outlet hole and decreasing the volume below it (fig. 2).

This understanding of physiology and governing variables explains why patients at the beginning of bleeding, (up to 10–12% of blood volume loss) maintain their

<sup>†</sup> Modified from references 27 and 28.

systemic hemodynamics well without changes in heart rate, blood pressure, or CVP, yet later, hemodynamics quickly deteriorate. The period of compensation reflects successful mobilization of  $V_u$  into  $V_s$ . Then, when the entire  $V_u$  has been mobilized, decompensation occurs suddenly. Similarly, when mobilization of  $V_u$  is secondary to an increase in sympathetic tone, an intervention associated with venodilation (general or regional anesthesia, opioids, sedatives), may cause rapid decompensation without additional blood loss because venodilation would be associated with a shift of volume from  $V_s$  back to  $V_u$ , resulting in a decrease in MCFP.

There is another interesting mechanism: Venous capacitance vessels are much more sensitive to sympathetic stimulation than arterial resistance vessels. Sympathetic stimulation of only 1 Hz results in a capacity response of almost 50% of maximal response observed during 20-Hz stimulation. On the other hand, the resistance response to 1 Hz stimulation is only 10% of maximum.<sup>2,34</sup> Clinical implications of this and other observations are that a response to a moderate increase in sympathetic tone (or a small dose of vasoconstrictors) is a constriction of capacitance (splanchnic) vessels which would expel blood from the splanchnic vasculature into the systemic circulation without a significant increase in systemic arterial resistance. On the other hand, the response to larger doses of vasoconstrictors would be associated with both decrease in venous capacity with recruitment of blood volume from splanchnic vasculature and an increase in arterial tone and blood pressure.

There is another important component in this picture: resistance within the splanchnic venous system. The main place of resistance to the venous flow out of the splanchnic vasculature is located within the hepatic veins<sup>15,35-37</sup> or within the liver itself.<sup>37</sup> One way or the other, an increase in resistance within the distal part of the splanchnic venous system would impede the outflow of blood from splanchnic organs, sequestering blood within the liver and more proximal parts of the splanchnic veins. Profound arterial hypotension during septic shock in piglets was not associated with a decreased MCFP but rather with a drastic increase in venous resistance within the distal part of the splanchnic vasculature.<sup>38</sup> A similar picture was observed in a porcine model of endotoxic shock.<sup>39</sup>

A decrease in resistance to venous flow within the liver and/or hepatic veins would facilitate the blood flow and volume shift from splanchnic vasculature to the inferior caval vein and right atrium, thereby increasing VR. Resistance within the liver and hepatic veins is mainly regulated by adrenergic receptors: Activation of  $\alpha$ -adrenergic receptors increases resistance,<sup>15,40</sup> whereas activation of  $\beta_2$ -adrenergic receptors decreases it, resulting in volume shift from the splanchnic vasculature into the systemic circulation.<sup>15,35</sup> Thus, the administration of pure  $\alpha$ -adrenergic agonists could result in a decrease in

venous capacity and an increase in  $V_s$  and MCFP, thereby increasing VR.<sup>40-54</sup> However, activation of  $\alpha$ -adrenergic receptors also could be associated with an increase in resistance within the liver and hepatic veins, which would impede the blood flow and shift of blood volume from the splanchnic system into systemic circulation.<sup>46,53-58</sup> In conditions of normovolemia and a relatively small degree of  $\alpha$ -adrenergic receptor activation, a decrease in venous capacity probably plays a more prominent role than an increase in resistance to the blood flow and volume shift from splanchnic vasculature. However, in conditions of hypovolemia (when further mobilization of  $V_u$  is decreased) and/or a high degree of  $\alpha$ -adrenergic receptor activation, sequestration of blood volume within the liver and further decrease in VR and CO may occur.<sup>53,54</sup> The combination of  $\alpha$ - and  $\beta_2$ -adrenergic agonists may facilitate the shift of blood volume from the splanchnic system into the systemic circulation more effectively than  $\alpha$ -adrenergic agonists alone: Such a combination would lead to a decrease in venous capacity, recruitment of  $V_u$  into  $V_s$ , and a decrease in resistance to venous outflow from the splanchnic system. Obviously, in conditions of severe hypovolemia, such shifts of blood volume would not be possible simply because of absence of  $V_u$  to be recruited; an increase in arterial pressure, if observed, would result mainly from  $\alpha$  receptor-mediated arterial constriction.<sup>53</sup> An increase in venous capacity by an  $\alpha$ -adrenergic agonist may also result from an activation of baroreceptors in the carotid sinuses secondary to an increase in arterial blood pressure.<sup>59,60</sup>

#### *Two-compartment Model of the Venous System*

Another important mechanism regulating the VR is resistance within the splanchnic arterial vasculature. Almost a century ago, the concept of a two-compartment model within the venous system was introduced<sup>61</sup>; one is very compliant and slow (splanchnic vasculature) and another is noncompliant and fast (nonsplanchnic venous vasculature; fig. 4, inside). This model has been used to explain many physiologic observations. It has also been periodically challenged.<sup>62</sup> However, as the reader will see, this theoretical model can logically and convincingly explain many observations regarding the behavior of venous system during one or another insult to cardiovascular function. The model can be described as follows: An increase in resistance in arteries and arterioles feeding compliant splanchnic veins decreases flow, pressure, and volume within splanchnic veins, shifting blood volume from the splanchnic veins into the systemic circulation, and *vice versa*, a dilation of these arteries leads to blood pooling within the splanchnic veins (fig. 3 and fig. 4, outside). Such shift of blood volume is reflected in a rapid increase in flow from the splanchnic vasculature into the systemic circulation. Such an increase in flow is transient and the resulting blood volume redistribution

would remain until the altered resistance in these arteries is maintained. When the change in resistance is reversed, the opposite shift of blood volume would occur.

Nonsplanchnic, less compliant veins behave differently. Dilation of small arteries and arterioles in the nonsplanchnic vasculature, if associated with a relatively minor or no decrease in arterial pressure, would increase VR (fig. 4, outside). Such an increase may be attributed to a few different mechanisms, including translocation of arterial blood centrally through the venous system as well as direct or more often indirect (*via* activation of the sympathetic nervous system and/or angiotensin system) constriction of veins leading to translocation of venous blood toward the heart; a simultaneous decrease in venous resistance within the distal part of the splanchnic venous vasculature may also play a role in such observations.<sup>63,64</sup> Finally and most importantly, a decrease in arterial resistance in the nonsplanchnic compartment, if associated with only a minor decrease in arterial pressure, leads to a significant increase in MCFP resulting from a decrease in the gradient between arterial and peripheral venous pressures increasing the MCFP and VR. This relation can be illustrated by an opening of a large arteriovenous fistula.<sup>28</sup> However, if a decrease in arterial resistance is associated with a significant decrease in arterial pressure, it could be associated with a decrease in MCFP and VR.

Hemodynamic response to exercise is a beautiful illustration of how the different vascular beds respond in opposite directions to fulfill the changing requirements of the body for blood volume and oxygen delivery redistribution. During exercise, splanchnic blood flow can reduce from 1,500 ml/min to 350 ml/min. Splanchnic oxygen consumption is preserved by an increase in arteriovenous oxygen difference in this region from 4 to 17 ml of oxygen/100 ml of blood.<sup>65</sup> On the other hand, total muscle blood flow can increase from approximately 1,000 ml/min at rest to almost 22,000 ml/min with an increase in CO to 25 l/min and oxygen uptake of almost 4 l/min. Arteriovenous oxygen difference in the muscle increases to 18 ml of oxygen/100 ml of blood, which represents approximately 90% oxygen extraction.<sup>66</sup> The mechanisms responsible for such hemodynamic adjustments involve different responses of the arteries and arterioles in the muscles *versus* the splanchnic system. An increase in sympathetic discharge during exercise leads to splanchnic arterial vasoconstriction leading to a decrease in flow, pressure, and volume within the splanchnic veins and an increase in VR and CO (fig. 3 and fig. 4, outside). The vasodilation within the exercising muscle, resulting to a minor extent from  $\beta_2$ -adrenergic receptor activation but mainly from a local accumulation of vasodilating metabolites (lactate, adenosine, and other compounds), leads to a decrease in arteriovenous pressure gradient in the muscle and a significant increase in MCFP, VR, and CO. Simultaneous

increase in sympathetic discharge constricts vasculature in nonexercising muscle and other tissues, helping to increase arterial pressure and MCFP, also increasing VR and CO. Additional mechanisms include "muscle pump" (during exercise contraction of muscles squeezes blood out of the muscles towards the heart), increase in heart rate and myocardial contractility, and many others.<sup>66</sup>

The effect of different vasodilators on VR and CO can depend on blood flow distribution between the two compartments, splanchnic and nonsplanchnic vasculature. For example, we and others observed that sodium nitroprusside decreases splanchnic blood flow.<sup>67,68</sup> Decrease in splanchnic flow should be associated with a decrease in pressure and volume within the splanchnic veins (fig. 3 and fig. 4, outside). However, it does not happen<sup>69,70</sup>: In another study, during similar degrees of arterial hypotension, vascular capacity was increased during sodium nitroprusside and to a greater extent during nitroglycerin-induced hypotension, whereas it was not changed during adenosine triphosphate administration.<sup>68</sup> That is, adenosine triphosphate and, to a lesser extent, sodium nitroprusside dilated nonsplanchnic arterial vasculature, leading to an increase in MCFP (due to a decrease in the pressure gradient between arteries and veins) and in VR. On the other hand, nitroglycerin dilated arterial vasculature within the splanchnic system, increasing flow, pressure, and splanchnic vascular volume and decreasing VR and CO (fig. 3 and fig. 4, outside). Active dilation of the splanchnic veins, in addition to the passive distention due to an increase in transmural pressure and volume, reinforces the accumulation of blood volume within the splanchnic venous system. Clinical observations support the notion that both sodium nitroprusside and nitroglycerin decrease arterial resistance and increase venous capacity.<sup>71</sup> However, it seems that sodium nitroprusside affects arterial resistance to a greater extent than venous capacity, whereas nitroglycerin increases venous capacity to a greater extent than decreases arterial resistance.<sup>71</sup>

Experiments using right heart bypass preparation, where blood flow and CVP were independently controlled and blood was drained separately from splanchnic and nonsplanchnic vasculature, demonstrated different effects of four vasodilators on splanchnic and nonsplanchnic arterial resistance.<sup>72</sup> The authors studied captopril, nifedipine, hydralazine, and prazosin in three doses that decreased arterial blood pressure to similar degrees. Captopril decreased arterial resistance, increased flow and volume within splanchnic vasculature, and decreased central blood volume; in the absence of bypass, it would lead to a decrease in VR and CO. Nifedipine did not affect arterial resistance within the splanchnic system but did significantly decrease it within the nonsplanchnic system. This was associated with a decrease in the pressure gradient between arterial and venous pressures within the nonsplanchnic system, and in-

creased MCFP and central blood volume, which in the absence of bypass would increase VR and CO. The differences in the effects of two remaining vasodilators were less drastic than the effects of nifedipine and captopril.<sup>72</sup>

The direct effects of vasodilators may be modified by indirect effects of mediators released during the administration of a drug in question. For example, isoproterenol administration is associated with an increase in norepinephrine release,<sup>73-77</sup> and that effect is mediated specifically *via*  $\beta_2$ - but not  $\beta_1$ -adrenergic receptors.<sup>78</sup> Isoproterenol also increases release of angiotensin.<sup>79</sup> As a result of such complexity, isoproterenol administration is associated with a drastic decrease in splanchnic and intrahepatic volume despite a significant increase in splanchnic blood flow.<sup>80</sup> According to the basic concepts of the relation between flow, pressure, and volume within the splanchnic vasculature (fig. 3), an increase in splanchnic flow should be associated with sequestration of blood volume within the splanchnic vasculature. In reality, this does not occur, and splanchnic volume significantly decreases.<sup>35,80</sup> Therefore, an increase in VR by blood volume shift from the splanchnic system results from a decrease in resistance within the liver and hepatic veins (mediated *via*  $\beta_2$ -adrenergic receptors), and venoconstriction, elicited by release of norepinephrine and/or angiotensin. Epinephrine increases VR mainly through activation of  $\beta_2$ -adrenergic receptors.<sup>59</sup> The role of an increased myocardial contractility (mediated *via*  $\beta_1$ -adrenergic receptors) in an increase in CO in a normal heart is probably minimal.<sup>53,59,78</sup>

#### *Intrathoracic Pressure*

An increase in intrathoracic pressure (ThorP) during controlled positive-pressure ventilation increases intramural CVP. This would decrease the pressure gradient for VR, VR itself, and blood volume in the right heart at diastole. On the other hand, every lung inflation moves the diaphragm downward, increasing intraabdominal pressure. The latter squeezes blood out of the veins within the abdominal cavity, increasing MCFP and VR, thereby helping to maintain the MCFP-CVP gradient and minimizing the effect of an increase in ThorP on VR.<sup>81</sup>

Reflexes and neurohumoral factors that increase MCFP also minimize the effects of increased ThorP on VR by an increase in arterial resistance within the splanchnic vasculature (leading to an increase in passive elastic recoil of splanchnic veins) and active venoconstriction; both result in a shift of blood volume from the splanchnic system into systemic circulation, increasing  $V_s$  and maintaining VR and CO. This shift is reinforced by an increase in intravascular volume secondary to antidiuresis (release of antidiuretic hormones).<sup>82-88</sup> An activation of the renin-angiotensin-aldosterone system during positive-pressure ventilation contributes to both mechanisms, namely an increase in MCFP by venoconstriction and an

increase in blood volume by water and sodium retention. An increase in intramural CVP during such a situation might be misinterpreted as hypervolemia and/or cardiac failure.

Finally, right ventricular filling pressure (defined as a gradient between CVP and pericardial pressure<sup>81</sup>) does not change during changes in ThorP because the right atrium, right ventricle, and pericardium are within the thorax, and an increase in ThorP is associated with equal increases in both right atrial and pericardial pressures. Therefore, absence of change in transmural right ventricular pressure during diastole further minimizes the effects of an increase in ThorP on VR. However, overinflation of the lung, introduction of positive end-expiratory pressure, and/or hypovolemia, present before introduction of controlled ventilation, might have exhausted the compensatory mechanisms and lead to a decrease in VR and CO.<sup>89</sup> An additional infusion of fluid and/or venoconstrictor might be needed to increase MCFP in order to maintain the necessary pressure gradient for VR.

During spontaneous inspiration, ThorP decreases, leading to a decrease in intramural CVP and a subsequent increase in gradient between MCFP and CVP, facilitating VR. However, an increase in VR secondary to a decrease in CVP works only when CVP is equal to or above atmospheric pressure because negative pressure in intrathoracic veins leads to their collapse, preventing a significant increase in VR. Also, pericardial pressure limits the overdistension of the right ventricle (see Pericardial Pressure section). If these mechanisms did not exist, forceful inspirations could lead to overextension of the right ventricle and its failure.<sup>31,81,90-93</sup>

**Systolic Blood Pressure and Pulse Pressure Variations.** During inspiration of positive-pressure ventilation, left ventricular stroke volume initially increases secondary to (1) temporary increase in left ventricular end-diastolic volume resulting from a compression of pulmonary veins, (2) decrease in afterload resulting from a decrease in left ventricular transmural pressure (*i.e.*, an increase in lung volume compresses the left ventricle and helps the left ventricular ejection), and (3) diminished right ventricular volume secondary to compression of the heart by inflated lungs. These factors lead to a temporary increase in left ventricular stroke volume, pulse pressure, and systolic blood pressure, compared with end of expiration (baseline). This deflection of blood pressure is called *delta-up* and usually is around 2-4 mmHg.<sup>94-96</sup> On the other hand, such inflation of the lung and an increase in ThorP decreases the pressure gradient for VR with subsequent decrease in VR. This in a few beats ends up with a decrease in left heart filling, in stroke volume of left ventricle and systolic pressure. This decrease in systolic pressure is called *delta-down*<sup>94,95</sup> and usually is around 5-6 mmHg. Total variation, *delta-up/delta-down*, thus is approximately 8-10 mmHg. If this variation is larger than that, it may reflect hypovolemia

and predict a positive response (an increase in CO) to additional fluid load. Systolic blood pressure variation not exceeding approximately 10 mmHg would reflect adequacy of ventricular preload<sup>15,94-99</sup> and may reflect the status of preload better than CVP.<sup>98</sup>

### *Intraabdominal Pressure*

Every inspiration, spontaneous or during positive-pressure breathing, moves the diaphragm downward, increases intraabdominal pressure, and shifts blood volume from the splanchnic system into the systemic circulation. At the same time, venous flow from the lower extremities along the inferior caval vein decreases. During expiration, the diaphragm shifts upward, decreases blood flow from the splanchnic system, and increases blood flow from the lower extremities. These cyclic events overall do not drastically affect VR and CO. However, a longer-lasting increase in intraabdominal pressure to any level lower than pressure within inferior caval vein may lead to a simultaneous increase in VR due to shift of blood volume from the compliant splanchnic venous system toward the right atrium; on the other hand, such an increase in intraabdominal pressure may decrease VR secondary to an increase in venous resistance within the inferior caval vein and to a shift of the diaphragm upward, an increase in ThorP with concomitant increase in intramural CVP.<sup>100-105</sup> Such an increase in CVP does not reflect the volume status of a patient<sup>106</sup> and may be associated with a decrease in VR<sup>100,101,107</sup> resulting from a decrease in the gradient between MCFP and CVP. This effect can be modified by an increase in  $V_s$ , which in turn can be achieved by an infusion of additional fluid and/or an administration of a vasoconstrictor.<sup>108</sup> Such intervention is not always needed because of the activation of sympathetic and renin-angiotensin systems; this is associated with an increase of MCFP and maintenance of the needed MCFP-CVP gradient to preserve VR and CO.<sup>103,109,110</sup> Anesthetics, sedatives, and other interventions might minimize such a homeostatic response.<sup>105,111-114</sup>

### *Positions (Tilts)*

Different positions, *e.g.*, head up *versus* head down, affect systemic hemodynamics including function of the venous system. A head-up position (*e.g.*, standing up) could be associated with a gravity-induced shift of blood volume from the upper to the lower part of the body. In healthy, awake patients, head-up or head-down positions do not affect blood pressure, CO, or CVP<sup>105</sup> because of immediate activation of sympathetically mediated reflexes as well as the renin-angiotensin system and release of other vasoconstricting mediators<sup>115</sup> prevent such a drastic shift of blood volume. However, during anesthesia, the head-up position is practically always associated with a decrease in CVP, CO, and blood pressure<sup>100,105,107,116</sup>

because the reflexes are blunted as the depth of anesthesia increases.<sup>105</sup>

The head-down (Trendelenburg) position is always associated with an increase in CVP. However, CO and blood pressure may be maintained<sup>37,100,107,115</sup> or decreased.<sup>105,116</sup> Left ventricular end-diastolic area (reflecting volume) and intrathoracic blood volume are increased.<sup>37</sup> After change from a head-down to a horizontal position in an anesthetized patient, a decrease in blood pressure and CO may occur.<sup>37</sup> It might be due to a failure to increase afterload or to hypovolemia which may have been misinterpreted as normovolemia or hypervolemia secondary to high CVP with the head-down position.<sup>105</sup>

### *Pericardial Pressure*

Any significant increase in VR (*e.g.*, during spontaneous inspiration) could lead to overloading of the right heart.<sup>117-121</sup> The limited rigid space of pericardium prevents overexpansion of the right heart.<sup>121</sup> In animals and humans, pericardectomy is associated with higher values of stroke volume and CO during exercise compared with similar exercises before pericardectomy.<sup>122</sup> Other mechanisms limiting overloading of the right heart include an increase in ThorP during controlled ventilation and, to a certain extent, during spontaneous expiration, as well as so-called ventricular interdependence<sup>121-125</sup>: An increase in right ventricular volume shifts the intraventricular septum leftward, leading to a decrease in left ventricular compliance, which decreases left ventricular filling, resulting a few beats later in a decrease in right ventricular preload.<sup>81</sup>

### *Role of Reflexes*

Many different pathophysiologic insults, *e.g.*, blood loss, the upright position,<sup>126</sup> initiation of positive pressure breathing, particularly with positive end-expiratory pressure, are associated with immediate increase in sympathetic discharge, which leads to an increase in arterial resistance, heart rate, and myocardial contractility and a decrease in venous capacity. The latter is particularly important: Capacitance vessels respond to hemorrhage much earlier than resistance vessels; both of these responses, arterial and venous, are mediated *via* the sympathetic nervous system. When the carotid sinus receptors sense low blood pressure, the sympathetic tone increases, splanchnic veins constrict,  $V_s$  and MCFP increase, and *vice versa*.<sup>2,10,19,127-133</sup> Pretreatment with the  $\alpha$ -adrenergic antagonist phentolamine decreased such response by 72%, whereas pretreatment with the  $\beta$ -adrenergic antagonist propranolol decreased such response by 35%. Combination of both decreased response by 73%. Therefore,  $\alpha$ -adrenergic mechanisms contribute more significantly to active changes in systemic venous capacity than the  $\beta$ -adrenergic system.<sup>134</sup> The responses to high or low arterial blood pressure are mediated not only through the carotid sinus but also

through the aortic baroreceptors. Their role in maintaining blood pressure is smaller than the role of the carotid sinuses.<sup>132</sup>

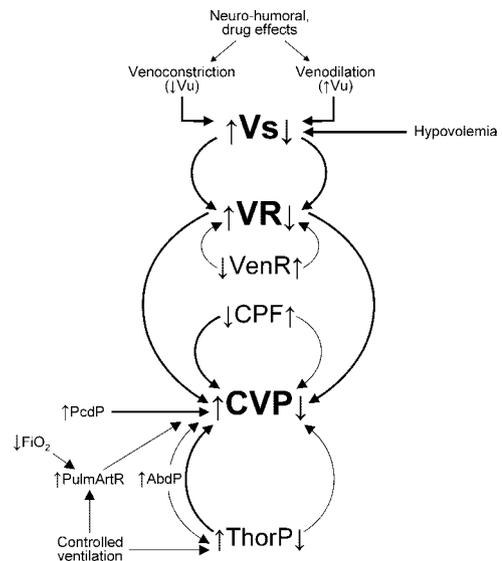
There are other types of reflexes, *e.g.*, an increase in intravenous volume and associated distension of the vein increases arterial resistance (upstream of the affected veins) *via* the so-called local sympathetic axon reflex or venoarterial reflex.<sup>135</sup> Teleologically speaking, this reflex helps to modify the degree of venous distention: Less blood inflow into a vein leads to a decrease in intramural pressure and volume (fig. 3).

### Is Central Venous Pressure a Useful or a Misleading Variable?

Values of CVP, intramural or even transmural, as well as values of pulmonary artery occluded pressure, do not correlate with the values of measured circulating blood volume or with responsiveness to fluid challenge (an increase in CO after infusion of fluid).<sup>99,136-143</sup> Moreover, attempts to assess the differences between the changes in CVP and changes in circulating blood volume also failed to find any significant correlation.<sup>144</sup> A sophisticated approach of measuring separately total blood volume and circulating blood volume, using a dye dilution technique, also did not demonstrate any correlation between values of CVP and blood volume, total or circulating (possibly total and stressed volumes).<sup>145</sup> Dramatic changes in systemic hemodynamics may not be associated with any significant changes in CVP, *e.g.*, significant decrease in mean arterial pressure and CO during high thoracocervical epidural and general anesthesia,<sup>146</sup> or drastic changes in arterial pressure, vascular resistance and venous capacity induced by changes in pressure within the carotid sinuses,<sup>147</sup> or a significant decrease in arterial resistance and an increase in CO induced by an infusion of prostaglandin E1<sup>148</sup> were not associated with any significant changes in CVP.

The main reason for lack of correlation between values of CVP and blood volume is that the body does everything possible to maintain homeostasis; an adequate transmural CVP is a must for cardiovascular function. The most accurate measurement of “volume status” would be the MCFP, which cannot be measured in a clinical setting.<sup>15</sup> Values of CVP depend on the relation between cardiac pump function and VR (determined by MCFP, Vs, venous resistance, and other factors) (fig. 5).<sup>139,149-154</sup> The pulmonary artery occluded pressure is an even worse indicator of volume status than CVP because it is far removed from the action of MCFP.<sup>15</sup> The pulmonary artery occluded pressure is a better indicator of left ventricular function than of volume status.<sup>15</sup>

Thus, considering the importance of maintaining the CVP adequate for cardiovascular function, it is not sur-



**Fig. 5. Variables affecting central venous pressure.** AbdP = intra-abdominal pressure; CPF = cardiac pump function; CVP = central venous pressure;  $F_{iO_2}$  = inspired fraction of oxygen; PcdP = pericardial pressure; PulmArtR = pulmonary arterial resistance; ThorP = intrathoracic pressure; VenR = venous resistance; VR = venous return; Vs = stressed volume; Vu = unstressed volume. *Thickness of the arrow* reflects the importance and/or relative frequency of influences in clinical practice. *Up and down arrows* represent increase or decrease of value of a function of a variable, respectively. The main factors that tend to decrease intramural and transmural CVP include venodilation (increase in Vu) and hypovolemia: Both may decrease CVP *via* a decrease in Vs and VR. Less important factors include an increase in VenR, an increase in CPF, and a decrease in ThorP. The main factors causing an increase in CVP include a decrease in CPF, a decrease in Vu, an increase in Vs, and an increase in ThorP and/or PcdP. Other factors include an increase in PulmArtR secondary to hypoxic hypoxia (decrease in  $F_{iO_2}$ ) or controlled ventilation. Controlled ventilation increases intramural (but not transmural) CVP *via* an increase in ThorP. An increase in AbdP may increase intramural and transmural CVP directly *via* a shift of blood volume from the splanchnic vasculature through inferior caval vein to the right heart and indirectly (only intramural CVP) *via* a shift of the diaphragm upward and associated increase in ThorP.

prising that values of CVP remain unchanged, despite serious stresses and changes in other cardiovascular variables. The correlation between CVP and circulating blood volume has never been found simply because it does not exist. To tease out when CVP may be useful or misleading, let us consider factors that affect CVP (fig. 5).

#### Factors That Decrease Central Venous Pressure

The main variable that tends to decrease intramural and transmural CVP is a decrease in Vs that can result from hypovolemia, which would initially lead to a decrease in Vu and shift of blood volume from Vu to Vs; when such shifts of volume exhaust the reservoir of blood volume, the Vu, Vs starts to decrease, eventually leading to a decrease in CVP. The second reason for a decrease in Vs is venodilation or, in other words, an increase in Vu; in this situation, blood volume shifts from Vs to Vu. A considerable decrease in Vs, whether it is

due to hypovolemia or venodilation, leads to a decrease in CVP secondary to a decrease in VR. Such a decrease initially would play a compensatory role because it would increase the pressure gradient between MCFP and CVP, mitigating the decrease in VR.

An isolated increase in venous resistance also may decrease intramural and transmural CVP secondary to a decrease in VR.<sup>155,156</sup> A decrease in ThorP (*e.g.*, during forceful inspiration) temporarily decreases intramural CVP resulting from negative pressure created within the thorax. This effect is not very powerful and is limited: During forceful inspiration, intrathoracic pressure decreases below zero, leading to collapse of large veins entering the thorax (waterfall phenomenon) and limiting the possible change in VR.

Nonetheless, if one observes a clearly noticeable decrease in CVP, it most probably reflects hypovolemia which exceeds 10–12% of blood volume loss, or venodilation associated with a shift of blood volume from  $V_s$  to  $V_u$ , *i.e.*, sequestration of blood within the splanchnic veins. Decreased CVP might also indicate an attempt by the heart to compensate for relatively mild hypovolemia: The heart would try to decrease CVP to increase gradient between peripheral and central venous pressures and to facilitate VR; therefore, the degree of hypovolemia might not correlate with the degree of a decrease in CVP. Clinically, it might be difficult to distinguish absolute hypovolemia from venodilation, which is hypovolemia relative to increased venous capacity. Overall analysis of the clinical course and appreciation of the difference between intramural and transmural pressures usually are helpful in such a differential diagnosis. Additional information such as stroke volume and CO can be crucially important in diagnosis of the pathophysiologic hemodynamic condition of a patient.

#### *Factors That Increase Central Venous Pressure*

The main factor that increases intramural and transmural CVP is a decrease in cardiac pump function, secondary to a decrease in contractility, valvular disease, dysrhythmias, *etc.* An increase in ThorP during ventilation, particularly with positive end-expiratory pressure, increases intramural (not transmural) CVP. Also, controlled ventilation increases pulmonary arterial resistance, which may increase intramural and transmural CVP. An increase in pulmonary arterial resistance can be caused by other reasons, including hypoxic pulmonary vasoconstriction, *e.g.*, secondary to a decrease in inspired fraction of oxygen, an increase in ventilation-perfusion abnormalities within the lung, an increase in pericardial pressure and/or in intraabdominal pressure, which might lead to an increase in intramural CVP through an increase in ThorP.

Venoconstriction (a shift of blood volume from  $V_u$  to  $V_s$ ) induced by an increase in sympathetic discharge and/or activation of the renin-angiotensin system, as

well as use of vasoconstrictors, also tends to increase intramural and transmural CVP. An increase in  $V_s$ , secondary to venoconstriction, or arterial/arteriolar constriction of splanchnic vasculature, or infusion of additional fluid, if associated with a decrease in cardiac pump function relative to an increased demand, would lead to an increase in intramural and transmural CVP. A high CVP, and CVP increasing during fluid load, indicates a heart problem rather than a circuit problem.

In clinical settings, intramural CVP often increases as a result of an increase in ThorP during controlled ventilation, particularly with positive end-expiratory pressure; transmural CVP may be close to normal. Some other physiologic insults may increase intramural and transmural CVP without heart problems; the Trendelenburg position, which increases CVP, is rarely harmful because of a concomitant increase in MCFP. The potential problem is that high CVP may lead to misdiagnosis of a patient's condition.

#### *Potential Misinterpretations of Normal Central Venous Pressure*

Correct interpretation of CVP values and changes in these values demand correct positioning of the transducer at the level of zero pressure all the time; periodic zeroing of the transducer is also needed. Normal CVP *per se* does not necessarily reflect normovolemia. The body can mobilize (and pool) blood volume from (or in) compliant splanchnic veins. Loss of 10–12% of blood volume does not decrease CVP. Normal CVP may reflect normovolemia or compensated hypovolemia (up to 600–700 ml of blood loss) or compensated hypervolemia: An excessive infusion of fluid may be compensated by accumulation of blood in the splanchnic veins without any change in central hemodynamics including CVP. Combination of factors that have a tendency to decrease and increase CVP may lead to a normal value of CVP despite serious hemodynamic derangements, *e.g.*, the combination of heart failure and hypovolemia, or hypovolemia in the Trendelenburg position. Drastic increases in MCFP and CO during exercise without any changes in CVP are well known.<sup>157,158</sup>

Therefore, considering the complexity of the physiologic feedback and clinical picture, robust reflexes, and homeostatic mechanisms (*fig. 5*), only at the extremes may CVP be a useful indicator of the hemodynamic state of a patient. An attempt to create a certain scoring system that takes into account almost all clinically available hemodynamic variables failed to identify CVP as a useful indicator.<sup>159</sup> The authors concluded that only extreme values of CVP may have clinical significance.

#### *Dynamic Variables That Reflect Volume Status*

Respiratory variations in CVP (namely a decrease in CVP during spontaneous inspiration) were relatively acceptable predictors of the CO response to fluid chal-

lence.<sup>154,160,161</sup> Other dynamic variables, such as systolic pressure variations, pulse pressure variations,<sup>139</sup> respiratory variations in pulse oximetry plethysmographic waveform amplitude,<sup>143</sup> and just a CVP and/or CO response to fluid challenge, are better indicators of volume status<sup>151</sup> than static hemodynamic variables including CVP. Critical analysis of the literature suggests a similar conclusion, that the inspiratory decrease in CVP (a dynamic variable) exceeding 1 mmHg is a much better predictor of responsiveness of CO to fluid challenge than CVP *per se*.<sup>138</sup>

A force applied to the abdomen with relaxed abdominal muscles is usually associated with a temporary increase in CVP resulting from blood volume shift from compressed splanchnic veins into the systemic circulation. This increase under normal situations is temporary because a normal heart responds to an increase in preload with an increase in contractility and temporary increase in CO. This increase in CVP lasts a few seconds, usually less than 10 s.<sup>162</sup> This is called *hepatojugular reflux*. Absence of such an increase in CVP might mean that splanchnic venous vasculature is relatively empty and there is no temporary increase in preload. If an increase in CVP lasts much longer than 10 s, it probably attests to some right or left ventricular insufficiency or both.<sup>162</sup> Passive leg raising can predict fluid responsiveness (an increase in pulse pressure) with 97% sensitivity and 94% specificity.<sup>163</sup> The Trendelenburg position is probably less telling than passive leg raising because the latter compresses the abdomen, squeezing the splanchnic vasculature and transferring blood into the systemic circulation. Many observers believe that these dynamic variables are more useful in identifying hemodynamic problems, particularly hypovolemia, than CVP.

Understanding the complexity of the function of the cardiovascular system in general and the venous system specifically, and an appreciation of the limitation of one or another hemodynamic variable including CVP, would help to properly diagnose the pathophysiologic condition of a patient and help to plan and execute appropriate therapeutic intervention.

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