Concise Definitive Review

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Role of the Venous Return in Critical Illness and Shock: Part II—Shock and Mechanical Ventilation

Duane J. Funk, MD[1,2]; Eric Jacobsohn, MD[1,2]; Anand Kumar, MD[1,3]

Objective: To provide a conceptual and clinical review of the physiology of the venous system as it is related to cardiac function in health and disease.

Data: An integration of venous and cardiac physiology under normal conditions, critical illness, and resuscitation.

Summary: The usual clinical teaching of cardiac physiology focuses on left ventricular pathophysiology and pathology. Due to the wide array of shock states dealt with by intensivists, an integrated approach that takes into account the function of the venous system and its interaction with the right heart may be more useful. In part II of this two-part review, we describe the physiology of venous return and its interaction with the right heart function as it relates to mechanical ventilation and various shock states including hypovolemic, cardiogenic, obstructive, and septic shock. In particular, we demonstrate how these shock states perturb venous return/right heart interactions. We also show how compensatory mechanisms and therapeutic interventions can tend to return venous return and cardiac output to appropriate values.

Conclusion: An improved understanding of the role of the venous system in pathophysiologic conditions will allow intensivists to better appreciate the complex circulatory physiology of shock and related therapies. This should enable improved hemodynamic management of this disorder. (*Crit Care Med* 2013; 41:573–579)

Key Words: cardiogenic shock; cardiovascular physiology; hemodynamics; hemorrhagic shock; obstructive shock; septic shock

Many, if not most, clinicians approach the management of acute cardiovascular dysfunction and shock using an analysis that emphasizes left ventricular physiology, probably as a consequence of medical training that emphasizes the role of left ventricular dysfunction in ischemic heart disease, the most common cause of death in the developed world. Intensivists deal with a broader array of cardiovascular perturbations including shock states in which vascular dysfunction and other extracardiac perturbations may dominate the clinical picture (e.g., septic, hypovolemic, or obstructive shock). In the first part of this two-part review, we reviewed an approach to cardiovascular physiology that incorporates both cardiac and vascular elements that may be more useful to intensivists than one that focuses exclusively on left ventricular physiology. In the second part of this review, we describe various shock states and how the knowledge of venous return (VR) and cardiac output (CO) curves help to diagnose and treat the common hemodynamic problems encountered in critical care. The key concepts described here are covered in detail in the first part of the review. The reader is encouraged to read that earlier physiologic review before proceeding with this current pathophysiologic review.

To review, only a portion of the total blood volume (V_t) contributes to the pressures generated in the circulation (1–6). The unstressed intravascular volume (V_o) can be defined as that volume required to fill the circulatory system to capacity without any increase in cardiovascular transmural pressure. Stressed volume (V_s) would be that amount which, when added to the unstressed volume, generates the cardiovascular transmural pressure. Passive exsanguination of an anticoagulated experimental animal would result in a large blood loss. The external, exsanguinated volume would represent the V_s. The amount remaining in the circulation would be V_o.

The mean systemic pressure (P_{ms}) is the average pressure throughout the entire circulatory system (cardiac/arterial/capillary/venous). It is most easily measured when pressures are equilibrated during brief cardiac standstill (2, 7). During active circulation, the portion of the cardiovascular circuit that has a pressure equivalent to P_{ms} is found in the small veins/venules in the splanchnic bed. P_{ms} can therefore be considered the upstream pressure driving VR ($VR = P_{ms} - P_{RA}/R_V$, where P_{RA} is right atrial pressure and R_V is venous resistance). Another salient point is that the R_V is represented by the inverse of the slope of the VR curve in the graphics attached to this article.

[1] Section of Critical Care Medicine, Department of Medicine, University of Manitoba, Manitoba, Canada.

[2] Department of Anesthesiology and Perioperative Medicine, University of Manitoba, Manitoba, Canada.

[3] Section of Critical Care Medicine, Cooper University Hospital, Cooper Medical School of Rowan University, Camden, NJ.

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For information regarding this article, E-mail: akumar61@yahoo.com

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VR AND CO IN PATHOPHYSIOLOGIC STATES

Hypovolemia

The changes in cardiac function and VR curves during hypovolemia and hypovolemic shock are shown in **Figure 1**. The normal circulatory state is represented by point A on the graph where the cardiac function (describing CO over a range of right atrial pressures) and VR curves (describing VR over the same right atrial pressure range) intersect. With the acute onset of hypovolemia, total volume (V_t) and stressed volume decrease, mean systemic pressure (P_{ms}) decreases, and the VR curve is shifted to the left (8). Consequently, it intersects the CO curve at a lower point and the net result is a decrease in VR/CO (point A to B). Note that this shift from point A to B does not take into account a sympathetic/endogenous catecholamine-driven compensatory increase in cardiac contractility (i.e., the slope of the ventricular function curve remains unchanged) or venous resistance (i.e., the slope of the VR curve remains constant).

A variety of compensatory responses that maintain CO/VR must then be considered. First, P_{ms} is supported through several mechanisms. Endogenous catecholamines from both sympathetic nerves and the adrenal medulla cause an early constriction of venous capacitance vessels with a resultant shift of intravascular volume from unstressed volume (V_o) to stressed volume V_s (6). In addition, a slow shift of interstitial fluid into the vascular compartment occurs. As a consequence of an increase in precapillary resistance and a decrease in postcapillary resistance with an enhanced production of plasma oncotic proteins under physiologic stress, a transfer of fluids from the interstitial to the intravascular compartment occurs (9). This results in a partial correction of V_t and V_s. Although both processes begin immediately, clinically significant volume transfers (on the order of hundreds of milliliters of fluid) take 6 to 12 hrs and peak responses (> 0.5 L) occur within about 3 days depending on the blood volume loss (10, 11). If the hypovolemia remains uncorrected, these compensatory changes would result in the shift of V_s, V_t, P_{ms}, and the VR curve back toward normal over hours and days (shown in Fig. 1 as the shift from point B back to point C). The second compensatory mechanism that occurs in hypovolemia is the secretion of endogenous catecholamines. This results in an early upward and leftward shift of the ventricular function curve (shown in Fig. 1 as the change from point C to D). This allows for maintenance of near-normal CO with moderate degrees (< 15% total volume) of blood loss.

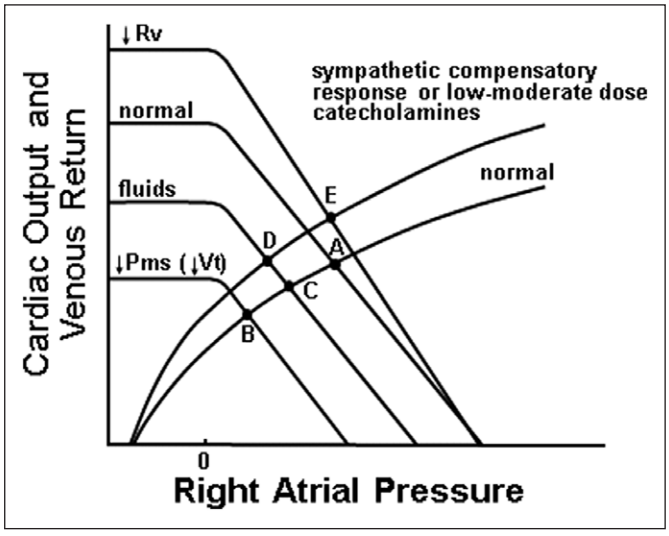

Figure 1. Hypovolemia and hypovolemic shock. *Arrows* indicate increase or decrease in parameter as appropriate (see text for explanation). Note that all figures in this review are illustrative and drawn to optimally demonstrate the key concepts. In particular, they are not meant to imply an absence of a plateau in the cardiac function curve with increasing filling pressures. P_{ms} = mean systemic pressure; V_t = total intravascular volume.

The obvious treatment of hypovolemia is the restoration of adequate P_{ms} by the administration of intravenous fluids, initially in the form of crystalloid. In Figure 1, this can be represented by the same shift on the curve from point B to C (which also represents the response to compensatory fluid shifts mentioned previously). Because V_t and V_s are increased, P_{ms} is partially restored, and the resultant CO/VR can be higher than baseline (Fig. 1, point C to D) due to the endogenous catecholamine-induced increase in cardiac contractility. This therapy also has the immediate effect of decreasing R_V due to an improvement in red blood cell rheology/fluid viscosity with hemodilution (because hemoglobin level is the primary determinant of blood viscosity). Later, R_V may also be decreased as a consequence of vasodilatation due to circulating mediators and NO (12–14). These effects can cause a shift of the restored VR curve to a steeper slope and an increase in CO/VR (Fig. 1, point D to E). The steeper ventricular function curve associated with catecholamine stimulation and the decrease in resistance to VR (R_v) with hemodilution explain why CO/VR can be increased above the baseline with small or moderate (typically < 15% total blood volume) degrees of hemorrhage treated with fluid resuscitation.

As noted previously, the transfer of blood from V_o to V_s in moderate hypovolemia can result in the maintenance of near-normal CO and mean arterial pressure (MAP). The reserve of the patient, however, is substantially decreased, and further significant losses of intravascular volume may result in a substantial decrease in VR/CO and MAP. This is clearly demonstrated when trauma patients are anesthetized. In addition to their adverse effects on myocardial contractility, almost all the anesthetic induction agents cause a significant increase in venous capacitance (i.e., a decrease in the proportion of V_s to V_o, in relation to a fixed V_t). In hypovolemic patients, this can lead to profound depression of VR/CO and MAP with a high risk of death.

Often, clinicians treating a hypovolemic, hypotensive patient will administer vasopressors to maintain normal blood pressure while there is ongoing fluid resuscitation. Depending on the choice of vasopressor, this may actually have a detrimental effect on CO. The administration of a pure α-agonist such as phenylephrine will generate a shallower slope of the VR curve, and result in a decrease in CO, but with maintenance of near-normal blood pressure. This may be useful for brief periods to

maintain blood pressure in a range that allows effective autoregulation of flow to vital organs.

Cardiogenic Shock

There are a variety of etiologies that can cause cardiac failure and cardiogenic shock. Most, including increased afterload, depression of myocardial contractility (ischemia, infarction, and others), arrhythmias, and mechanical valve failure affect VR in similar ways in that they increase P_{RA}. This decreases the driving pressure gradient ($P_{ms} - P_{RA}$) for venous flow and reduces VR, which directly limits CO.

As seen in **Figure 2**, cardiac failure and cardiogenic shock shift the cardiac function curve downward and to the right (flatter curve) due to decreased contractility. The resulting intersection with the VR curve occurs at a lower than normal CO (Fig. 2 point A to B). Note that at point B, P_{ms} (the intercept of the VR curve with the abscissa) is unchanged and although P_{RA} is substantially higher than normal, VR/CO is markedly lower. In Figure 2, P_{RA} is the line drawn perpendicular from point B to the abscissa of the graph. This is in contrast to the effect of fluid loading which increases P_{ms}, VR/CO, and P_{RA}. As noted earlier, the higher P_{RA} reduces the gradient for blood flow to the right atrium. Thus, despite a higher P_{RA} and measured central venous pressure in this condition, VR/CO is reduced.

The compensatory release of endogenous catecholamines causes an increase in V_s relative to V_o with a resulting increase in P_{ms} (6). Administration of fluid also increases P_{ms} by increasing V_t and V_s without a change in V_o. Both generate a similar rightward shift of the VR curve (viscosity effects are ignored). However, because a large degree of myocardial dysfunction results in a ventricular function curve that is substantially flattened, the beneficial impact of any increase in P_{ms} from fluid administration or sympathetic activation will be modest (Fig. 2, point B to C). Further fluid administration would not substantially increase CO, but would only increase pulmonary venous pressure and lead to the formation of pulmonary edema. If cardiac contractility is less severely depressed (with a better maintained and steeper cardiac response curve), the initial decrease in CO/VR will be less and the effect of modest fluid administration may be sufficient to restore it to a normal range.

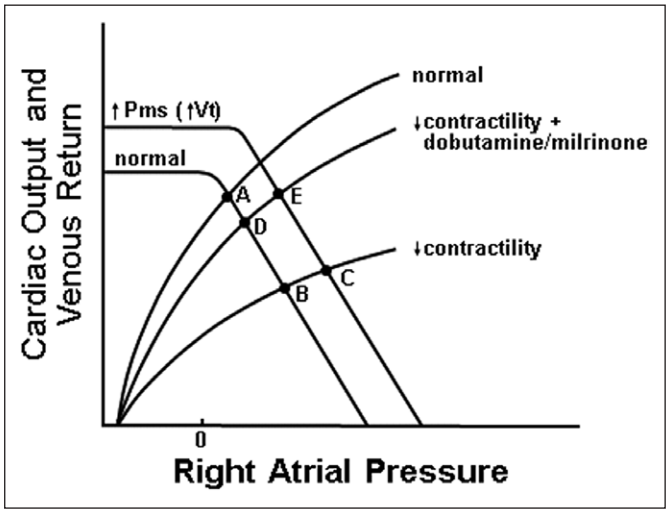

Figure 2. Cardiac failure and cardiogenic shock. *Arrows* indicate increase or decrease in parameter as appropriate (see text for explanation). P_{ms} = mean systemic pressure.

The use of inotropic agents is a standard therapy of cardiac failure and cardiogenic shock of almost any etiology. The most common agents used are dobutamine, a synthetic catecholamine, and milrinone, a phosphodiesterase inhibitor. Both have similar effects on the cardiovascular system, generating a moderate increase in cardiac contractility with a mild-to-moderate degree of arteriolar and venous vasodilatation (dependent on a lower range dose in the case of dobutamine [15–18]). Both effects are beneficial in cardiac failure. The increase in cardiac contractility and decrease in pulmonary vascular afterload generate a steeper Starling cardiac function curve. Used alone without concomitant fluids, a partial correction of a depressed Starling curve will yield a significantly improved VR/CO (Fig. 2, point B to D). However, assuming that V_s and P_{ms} are maintained or augmented with modest fluid support, the intersection of the curves moves CO/VR upward toward normal even if contractility remains somewhat depressed (i.e., the ventricular response curve remains shifted downward compared with normal) (Fig. 2, point D to E). In addition, the venous vasodilatory effect of both drugs will result in a decrease in R_v (i.e., a steeper VR slope, not shown in Fig. 2), which will further augment CO/VR again, assuming that V_s and P_{ms} are maintained with fluids as the natural effect of a vasodilator will be to decrease the proportion of V_s to V_o and decrease P_{ms}.

If cardiac injury is sufficiently severe, combined systolic and diastolic dysfunction shifts the ventricular response curve markedly downward (flatter) and to the right. This manifests as a substantial increase in P_{RA} that causes a narrowing of the P_{ms} to P_{RA} gradient. Because this gradient drives VR, decreased VR/CO will manifest and, if sufficiently severe, cardiogenic shock may result. In that circumstance, dopamine or norepinephrine, inotropic agents with robust inotropic and vasoconstrictive actions, are often required. These drugs, in contrast to milrinone and dobutamine, will tend to increase V_s as a portion of V_t. The net effect is to generate a more modest inotropic effect than dobutamine or milrinone while maintaining the robust vasopressor effects required in hypotensive shock patients (19).

Although ischemic cardiac injury is dominantly left-sided, such injury (from a myocardial infarction for example) will often also cause right ventricular dysfunction. In addition to the fact that there is often an element of direct RV injury with LV infarcts, all causes of left ventricular dysfunction result in increases in pulmonary artery pressures and RV afterload. This represents an impediment to right ventricular systolic ejection and results in a flattening of the right heart Frank-Starling relationship. In addition, the increased P_{RA} associated with RV dysfunction results in a narrowing of the VR gradient ($P_{ms} - P_{RA}$) and a decrease of VR/CO. As noted previously, in terms of venous physiology, this increase in P_{RA} is the only mechanism through which cardiac dysfunction can reduce VR.

Distributive Shock

Distributive shock is a generic term for a pathophysiologic state that combines hypotension with significant arteriolar and venous dilation. Altered distribution of blood volume and blood flow is also characteristic. Septic shock is the prototypical disease that causes distributive shock, although the other conditions found in critically ill patients may exhibit similar hemodynamic aberrations (systemic inflammatory response, anaphylactic/anaphylactoid responses, vasodilating drugs, liver failure, adrenal insufficiency, anaphylaxis, thiamine deficiency, carcinoid syndrome, etc.).

Activation of the inflammatory cascade as a result of severe infection leads to the release of endogenous mediators such as cytokines (tumor necrosis factor-α, interleukin-1β, etc.), eicosanoids (prostacyclins, prostaglandins, leukotrienes), and others (20, 21). Many of these factors drive up regulation of inducible nitric oxide synthase (NOS) producing nitric oxide, which is thought to be the end mediator of vascular smooth muscle relaxation throughout the cardiovascular system (22–26). The result is a reduction of R_v and P_{ms}. In addition, cytokine-mediated NOS activity may have a substantial role in the variable degrees of myocardial depression that is typically seen in sepsis and septic shock (27, 28). A graphical representation of septic shock is depicted in **Figure 3**.

Early in the course of septic shock, P_{ms} decreases. One of the primary reasons is a shift of stressed volume (V_s) to unstressed volume (V_o) as a consequence of increased venous capacitance resulting from active dilation of small venules/veins. This increase in unstressed volume (V_o) and decrease in stressed volume (V_s) have been confirmed in experimental animal models of canine and porcine endotoxemia (29–31). Furthermore, total circulating volume (Vt) and stressed volume (V_s) may both be decreased due to loss of fluids to the interstitium, increased insensible losses, and decreased oral intake. As a consequence of the decreased P_{ms} in early, unresuscitated septic shock, VR, and CO are often reduced (Fig. 3, point A to B). Septic shock is also associated with dilatation of large veins and shunting of arterial blood flow to low resistance (fast time constant) vascular beds (as described in part I of this review), both of which decrease R_V and augment VR (31, 32). Hemoconcentration due to increased fluid loss to the interstitium, increased insensible losses, and decreased fluid intake may generate increased blood viscosity, attenuate the decrease in R_V, and limit augmentation of VR (30). Overall, despite hemoconcentration, R_V decreases and the slope of the VR curve becomes steeper (Fig. 3, point B to C). However, the decreased R_v typically does not fully compensate for the decreased P_{ms} in unresuscitated septic shock, and hence CO usually remains depressed. At this unresuscitated stage of septic shock, the physical examination frequently is suggestive of a hypodynamic, low CO condition. The patient will often be cold and clammy with a narrowed pulse pressure (hypodynamic shock). Central and mixed venous oxygen saturations are often low at this stage (33–35).

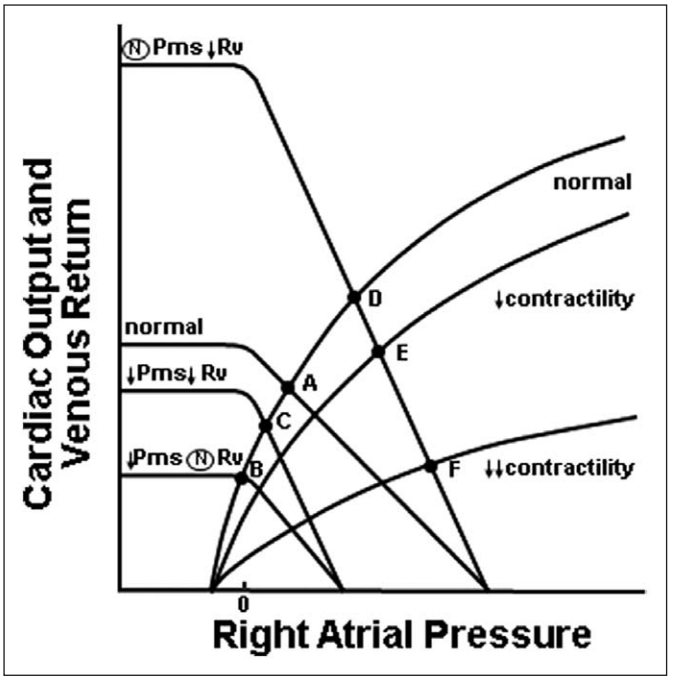

Figure 3. Septic shock. *Arrows* indicate increase or decrease in parameter as appropriate. Circled "N" indicates "normal" (see text for explanation). P_{ms} = mean systemic pressure; R_v = venous resistance.

Subsequently, fluid resuscitation in septic shock generates a marked augmentation in V_t. Although 5 to 10 L of crystalloid over 24 hrs is often provided in clinical practice (36, 37), a significantly smaller volume on the order of 0.5 to 2 L is probably sufficient to sufficiently augment V_t (35, 38). Fluid resuscitation results in a correction of V_s and P_{ms} back to normal (or potentially higher), allowing the decreased R_v (with steeper VR curve) to be manifested by increased VR/CO (Fig. 3, point C to D) that can be more than double normal (31). The hyperdynamic circulation may be further accentuated by a further decrease in R_V related to hemodilution and decreased blood viscosity (not shown in figure). This classical hyperdynamic (high CO/low SVR) hemodynamic picture of established septic shock typically does not manifest without fluid resuscitation (39–42). However, even a modest degree of fluid resuscitation may be sufficient to allow the permissive effects of the decreased R_v to be expressed as increased CO.

Based on echocardiography and radionuclide ventriculography, the majority of patients with septic shock also develop a degree of biventricular myocardial depression as manifested by a decreased ejection fraction (with biventricular dilatation (43–45)). However, the decreased R_v in the context of restored V_s due to fluid resuscitation normally overshadows the depressed contractility so that patients remain substantially hyperdynamic with increased VR/CO. These effects are illustrated in Figure 3 (point D to E). In a small subset of patients, myocardial depression is sufficiently severe that VR/CO remains decreased even after resuscitation (Fig. 3, point F). In this situation, an emphasis on inotropic support rather than the more typical vasopressor approach to therapy may be required.

Obstructive Shock

There are several pathophysiologic phenomena that cause obstructive shock. Conditions such as tension pneumothorax,

pericardial tamponade, or compression of the inferior vena cava secondary to abdominal compartment syndrome or pregnancy can all cause a decrease in CO due to obstructive shock. Large pulmonary emboli can also cause a form of obstructive shock that acts very similarly to cardiogenic shock. Given its interesting and complex pathophysiology, tension pneumothorax will be examined as an example of obstructive shock.

Tension pneumothorax causes a reduction in the VR because of an increase in intrathoracic pressure. As we can see in **Figure 4**, several changes occur in the VR and cardiac function curves with the development of a tension pneumothorax.

The primary pathophysiologic event in the development of obstructive shock due to tension pneumothorax is that an increasingly positive pleural pressure (P_{PL}) and not P_{RA} becomes the limiting factor of blood flow to the right heart (46, 47). When P_{PL} exceeds P_{RA}, the numerator of the VR equation ($VR = P_{ms} - P_{RA}/R_v$) becomes $P_{ms} - P_{PL}$. VR no longer increases with a decrease in P_{RA}. Normally, VR plateaus as P_{RA} approaches P_{atm}. With tension pneumothorax, the limitation of VR occurs at P_{PL} (i.e., a value greater than P_{atm} where $P_{RA} = 0$). Assuming that P_{ms} and R_v are unchanged, this results in a VR curve where the inflection of the plateau point is shifted downward and to the right (with a down-shifted plateau) but where the slope ($1/R_v$) and the x-axis intercept (P_{ms}) are unchanged. In the absence of other effects, a physiologic impossibility would result; the intercept of the cardiac function curve and the VR curve (defining VR/CO) would shift to the plateau portion of the VR curve with only a modest depression of VR/CO (Fig. 4, point A to A_1). This is not possible because there can be no ventricular volume when intrathoracic pressure (reflected by P_{PL}) exceeds intraventricular pressure (reflected by P_{RA}) as occurs at this theoretical point.

However, as part of the response to increased P_{PL}, the cardiac function curve is shifted rightward on the graph. This rightward shift occurs as a consequence of the fact that the presence of an increased pleural pressure adversely impacts effective cardiac compliance. Diastolic ventricular distension (preload) and the Starling response are dependent on the cardiac transmural pressure gradient. When P_{PL} increases with a tension pneumothorax, the transmural pressure gradient narrows and ventricular filling is impaired. Ventricular filling can be maintained but at a significantly higher filling pressure (P_{RA}). This effect shifts the ventricular function curve to the right. In this situation, VR/CO will transition from point A to B (rather than A_1) as shown in Figure 4.

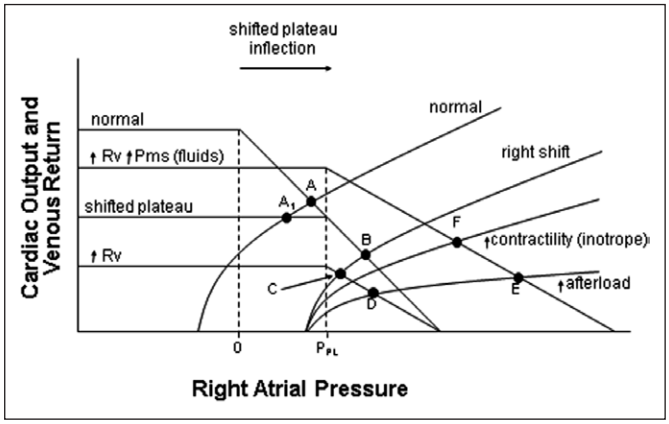

Figure 4. Tension pneumothorax as an example of obstructive shock. *Arrows* indicate increase or decrease in parameter as appropriate (see text for explanation). P_{ms} = mean systemic pressure; R_v = venous resistance; V_s = stressed volume.

Several other hemodynamic pathophysiologic events occur. The increase in P_{PL} causes compression of the large veins in the thorax increasing R_v. The result is a shallower slope in the VR curve, which further depresses VR/CO (Fig. 4, point B to C).In addition to the rightward shift of the cardiac function curve, the curve is flattened as a consequence of a substantial increase in RV afterload secondary to lung collapse and acute hypoxemia (which increases pulmonary vascular resistance) induced by the pneumothorax (47). This further reduces VR/CO (Fig. 4, point C to D).

There are significant compensatory responses that are not shown graphically in the interests of simplicity. Endogenous catecholamine release results in a shift of V_o to V_s without an alteration in V_t resulting in an increase in P_{ms}. This effect may be partially offset by vasoconstriction of large veins and the vena cava resulting in a higher R_v and a shallower VR curve. In addition, this stress-associated sympathetic catecholamine surge will tend to increase contractility resulting in a steeper Starling response curve although it will not offset the increase in right ventricular afterload.

Temporizing therapies may prove useful depending on the degree of hemodynamic compromise. The first therapy applied is often intravascular expansion with resuscitative fluids, which increases V_t, V_s, and P_{ms} shifting the VR curve to the right so that it intercepts the cardiac contractility curve at a somewhat higher CO/VR (Fig. 4, point D to E). This may be effective if the pneumothorax is associated with only a modest increase in P_{PL}. However, the administration of large amounts of fluid will result in a negligible increase in VR/CO despite substantial increases in P_{ms} if the cardiac function curve is markedly flattened by the increased right ventricular afterload. If fluid administration results in an insufficient response, an inotropic agent is often initiated. The combination of fluids and inotropic support may be more effective than either therapy alone (Fig. 4 point E to F). However, despite such aggressive cardiovascular support, CO/VR rarely achieves normal values except in the early stages of hemodynamic compromise. In addition, fluid therapy is limited by the increase in capillary filtration that will occur with the increase in hydrostatic pressure from administering excessive volume. Further in the pathophysiologic progression of this condition, supportive modalities are unable to shift the curves sufficiently and only decompression will be effective.

If the hypotension that is often seen with a tension pneumothorax is treated with a pure vasopressor (such as phenylephrine), the result will be a further decrease in CO/VR because of the increase in R_V and, potentially, increase in pulmonary afterload.

When pericardial tamponade is the cause of obstructive shock, the same physiologic principles as in tension pneumo-

thorax apply. The difference being that the impedance to VR is now pericardial pressure (P_{Per}) as opposed to P_{PL} and the numerator for the VR equation becomes $P_{ms} - P_{Per}$. As with tension pneumothorax, the initial use of fluids and inotropes will have modest effects on improving CO but with pathophysiologic progression, only decompression of the tamponade will be effective.

Effect of Positive Pressure Ventilation on VR and Cardiac Function

The effects of mechanical ventilation on cardiac function and VR are similar in nature to tension pneumothorax, but generally less in magnitude. As seen in **Figure 5**, institution of positive pressure mechanical ventilation causes analogous changes (when compared with tension pneumothorax) in the VR and cardiac function curves that can, on occasion (and depending on cardiac function and volume status), result in hypotension. Upon switching from negative pressure ventilation to positive pressure ventilation, R_V increases (a shallower slope of the VR curve) because of the compression of the intrathoracic veins and vena cava. The result is the shift from point A to B in Figure 5. In addition, mean positive intrathoracic pressure caused by mechanical ventilation results in a rightward shift of the right heart ventricular function curve as a consequence of decreased effective cardiac compliance. The curve is also somewhat depressed/flattened due to the increased right ventricular afterload due to increases in pulmonary vascular resistance caused by the positive intrathoracic pressure (Fig. 5, point B to C).

Although endogenous catecholamine release will reverse some of these changes, the standard therapy of fluid infusion is often needed to return CO/VR to normal range (Fig. 5, point C to D). However, CO/VR compromise may be especially profound if the patient is already volume depleted with a low P_{ms} (Fig. 5, point C to E) or if intrathoracic pressure is markedly increased (high levels of positive end-expiratory pressure [PEEP] or auto PEEP in association with chronic obstructive pulmonary disease/asthma) which results in both an increase in R_V (not shown) and more profound shift and depression of the cardiac function curve (Fig. 5, point C to F). Interestingly, in drawing a line perpendicular from point C to the abscissa/x-axis of the VR graph (the intersection representing P_{RA}) and a similar line from point A to the abscissa, it is apparent that under positive pressure ventilation P_{RA} actually increases despite a decrease in CO/VR. This is part of the reason why static predictors of preload such as P_{RA} are inadequate in predicting CO and volume responsiveness in mechanically ventilated patients (48–53).

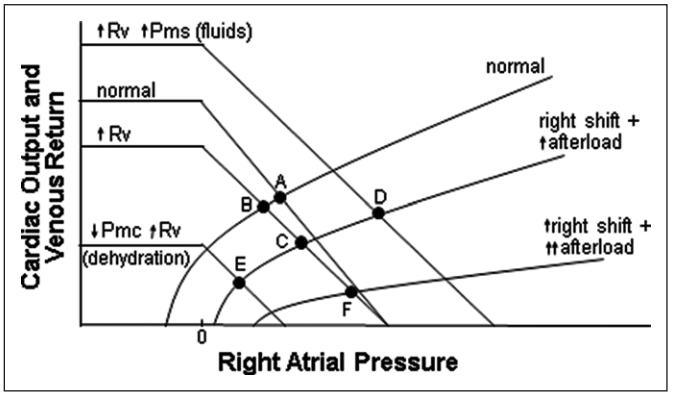

Figure 5. Effect of mechanical ventilation. *Arrows* indicate increase or decrease in parameter as appropriate (see text for explanation). P_{ms} = mean systemic pressure; R_v = venous resistance; $V_{s=}$ stressed volume.

CONCLUSIONS

The understanding of circulatory physiology is paramount to the treatment of the critically ill. The traditional approach has been to focus on the left heart and the factors that govern left heart CO. As the reader has seen, there are many forms of shock that involve alterations in the vasculature or other extracardiac perturbations. It is in these cases that the concept of VR plays an important role in the understanding and treatment of these complex patients.

The initial description of the role of the vasculature in regulating CO over 115 yr ago by Bayliss and Starling and further delineated by Guyton in the 1950s still has clinical relevance today when managing patients with complex pathophysiology.

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