CASE 12

A 25-year-old pregnant woman is in labor at the hospital. She has no medical problems and has had no complications with this pregnancy. She is in the active phase of labor, feeling intense contractions, and wants pain relief. The anesthesiologist is called and administers an epidural nerve block (including sympathetic blockade) for anesthesia. Shortly after the administration of the epidural, the patient reports feeling light-headed and dizzy. She is noted to be tachycardic (rapid heart rate) and hypotensive (low blood pressure). The anesthesiologist notices the hypotension and gives an intravenous (IV) fluid bolus and a small amount of IV ephedrine. These measures resolve the patient’s symptoms and hypotension.

◆ Why would epidural analgesia cause these symptoms?

◆ How would increasing the blood volume change venous pressure (VP)?

◆ How would ephedrine counter the hypotension?
ANSWERS TO CASE 12: REGULATION OF VENOUS RETURN

Summary: A 25-year-old pregnant woman in active labor develops hypotension and tachycardia after epidural analgesia is administered.

- **Effects of the epidural:** Sympathetic blockade resulting in decreased VP, and thus decreased cardiac output (CO), and decreased peripheral resistance resulting in hypotension.

- **Increase in blood volume:** Increases venous pressure.

- **Giving ephedrine:** Increases $\alpha_1$ stimulation, leading to contraction of the venous musculature, increasing VP and thus CO and peripheral resistance.

**CLINICAL CORRELATION**

When using any medication, one must be able to anticipate potential adverse effects and be prepared to address them if they occur. This is evident with the epidural anesthesia often used in labor and delivery and in other types of surgeries for pain relief. The pain relief that results from blocking afferent nerves that innervate the uterus (T10 to L3) is associated with a sympathetic blockade that in turn affects venous tone and peripheral resistance. When the sympathetic system is blocked, there is relaxation of venous and arteriolar smooth muscle, resulting in increased unstressed volume and decreased total peripheral resistance (TPR). These changes result in decreased VP, CO, and mean arterial pressure. Clinically, the drop in mean arterial pressure results in tachycardia if sympathetic innervation to the heart is not blocked. CO is calculated by multiplying the heart rate by the stroke volume, and so to try to maintain CO, the body compensates by increasing the heart rate. Anesthesiologists are aware of this complication and preload patients with isotonic IV fluids (500-1000 mL) before administering the epidural. This preload will increase VP by shifting the vascular function curve to the right, resulting in increased CO. If this preload is not enough, ephedrine often is given to increase venous smooth muscle contraction (decreasing unstressed volume), further increasing VP and CO. The increased CO, plus ephedrine’s actions to cause arteriolar constriction, thus increasing TPR, will combine to return mean arterial pressure toward control values.

**APPROACH TO PHYSIOLOGY OF VENOUS RETURN**

**Objectives**
1. Discuss the Frank–Starling relationship in terms of VP and CO.
2. Draw and label cardiac and vascular function curves.
3. Diagram the effects that changes in heart rate, contractility, blood volume, venous unstressed volume, and TPR have on the cardiac and vascular function curves and the resultant VPs and COs.
**Definitions**

**Venous return**: The volume of blood returning to the heart per minute.  
**Cardiac function curve**: Depicts the dependence of CO on VP.  
**Vascular function curve**: Depicts the dependence of VP on CO.

**DISCUSSION**

During a steady-state condition, CO and venous return are equal. The level of CO, and hence venous return, at any moment is determined by the interplay of factors that regulate cardiac function and factors that regulate vascular function. As can be seen in Figure 12-1, CO is a function of VP. The dependence of CO on VP is referred to as the Frank–Starling relationship and is displayed as a cardiac function curve. Blood that is flowing into the heart during diastole will stretch the muscle fibers. The volume of blood entering the heart depends on the VP driving the flow. The greater the VP (going from A to B), the more blood, the longer the muscle cell length, and the greater the force of contraction (see Case 10). Although CO is dependent on VP, the effect that a particular VP will have on CO is not constant. That is, there is not just one curve but a family of curves that adhere to the Frank–Starling relationship. The factors determining CO at any given VP are heart rate, myocardial contractility (see Case 11), TPR, and the pressure outside the heart (intrathoracic pressure).

The level of VP at any single moment is also determined by the interplay of factors that regulate cardiac function and factors that regulate vascular function.

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**Figure 12-1.** Cardiac output in relation to venous pressure. Going from A to B, an increased amount of blood enters the heart, stretching the cardiac muscle length and increasing the force of contraction. CO = cardiac output; VP = venous pressure.
As can be seen in Figure 12-2, VP is a function of CO. If the heart is stopped, blood will continue to flow from the arteries into the veins until the pressure is the same throughout the cardiovascular system. Thus, arterial pressure will fall and VP will rise. The final pressure is called the mean circulatory filling pressure (MCFP). Once the heart starts pumping again, VP decreases, with the magnitude of the decrease being greater the greater the CO. There is a limit to how high CO can go because of the fact that the veins will collapse at low VPs. This relationship between CO and VP describes a vascular function curve. Just as the relationship between VP and CO depends on other factors, so does the relationship between CO and VP. The MCFP (VP at zero CO) depends on blood volume and the state of contraction of venous smooth muscle (unstressed volume). The greater the blood volume and the greater the contraction of venous smooth muscle, the greater the MCFP. The slope of the vascular function curve depends mainly on TPR. The greater the TPR, the greater the fall in VP for any given increase in CO.

The results of the interplay of the cardiac function curve and the vascular function curve, along with the effects of changing the factors that influence those curves, can be illustrated and understood by combining the two curves. Usually the vascular function curve is flipped so that VP is on the x-axis and CO is on the y-axis as in Figure 12-3. The point where the two lines cross—the "equilibrium point" (A)—defines the CO and the VP that exist under the current conditions. Changes in any of the factors that affect the cardiac function curve and/or the vascular function curve alter both CO and VP.

Increases in heart rate, increases in myocardial contractility, and decreases in TPR all increase CO at any VP. This can be viewed by shifting the cardiac function curve upward to yield a new equilibrium point (B in Figure 12-3). Of course, opposite changes in heart rate, contractility, and TPR will decrease...
CO at any VP and would shift the curve downward. Increases in blood volume and contraction of venous smooth muscle increase VP at any CO. This can be seen by shifting the vascular function curve to a higher MCFP but keeping the slope the same, producing a new equilibrium point (C in Figure 12-3). Note that CO also is increased if factors affecting the cardiac function curve do not change. Decreases in blood volume and relaxation of venous smooth muscle, as occurred in this case, would have the opposite effect, a decrease in VP (and a decrease in CO if factors affecting the cardiac function curve do not change). The effects of changes in TPR alone are a little more difficult to understand and visualize. Increases in TPR do not change MCFP, but they do decrease VP at all other COs. This can be visualized by shifting the vascular function curve counterclockwise. Viewing this shift in combination with the shift that an increase in TPR has on the cardiac function curve indicates that there will be a decrease in CO (point D in Figure 12-3). This decrease in CO will moderate the increase in mean arterial pressure (MAP) that results from the increase in TPR.

**COMPREHENSION QUESTIONS**

[12.1] A patient exhibits an elevated jugular venous pressure. This could be the direct result of which of the following?

- A. Decreased blood volume
- B. Decreased myocardial contractility
- C. Increased heart rate
- D. Increased total peripheral resistance (TPR)
- E. Relaxation of venous smooth muscle

**Figure 12-3.** The equilibrium points indicate the CO and VP that exist under various conditions as described in the text. CO = cardiac output; VP = venous pressure.
A patient with a bleeding duodenal ulcer arrives at the hospital with a markedly low mean arterial pressure. In addition to the low MAP, this patient is likely to exhibit which of the following?

A. Decreased heart rate  
B. Decreased myocardial contractility  
C. Decreased TPR  
D. Decreased VP  
E. Increased CO

A 48-year-old male with malignant hypertension and a markedly elevated mean arterial pressure is given a drug that relaxes arterioles, thus reducing TPR. Which of the following is most likely to result from the reduction of TPR in this manner?

A. Decreased CO  
B. Decreased heart rate  
C. Decreased myocardial contractility  
D. Increased blood volume  
E. Increased VP

**Answers**

**[12.1]** B. Elevations in central VP can result from contraction of venous smooth muscle and increases in blood volume, but most often they are caused by defects in cardiac function such as a reduction in myocardial contractility. The direct effects of a decrease in myocardial contractility can be viewed on a combined vascular and cardiac function curve by shifting the cardiac function curve downward.

**[12.2]** D. Loss of blood will result in a decrease in MCFP and can be expressed as a decrease in VP and a decrease in CO. This will lead to a decrease in mean arterial pressure and a compensatory increase in heart rate, myocardial contractility, and TPR. The direct effects of a decrease in blood volume can be viewed on a combined vascular and cardiac function curve by shifting the MCFP to the left without changing the slope of the vascular function curve.

**[12.3]** E. A decrease in TPR will result in a shift of blood from the arterial side to the venous side of the circulation, thus increasing VP and CO without changing blood volume. The decrease in TPR most likely also will result in a decrease in mean arterial pressure and a compensatory increase in heart rate and myocardial contractility. The direct effects of a decrease in TPR can be viewed on a combined vascular and cardiac function curve mainly by shifting the slope of the vascular function curve upward. (Note that a decrease in TPR also will shift the cardiac function curve upward, but the effect is not enough to bring VP back to its initial value.)
PHYSIOLOGY PEARLS

❖ CO at any given VP is a function of heart rate, contractility, TPR, and intrathoracic pressure and is represented by the cardiac function curve.
❖ VP at any given CO is a function of blood volume, unstressed volume, and TPR and is represented by the vascular function curve.
❖ The CO and VP at any one time is the result of the interplay of those factors determining the cardiac and vascular functions curves.

REFERENCES

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