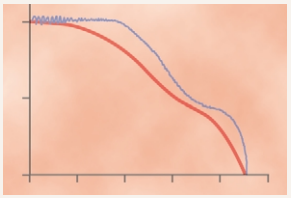
C H A P T E R 2 4

Circulatory Shock and Physiology of Its Treatment



Circulatory shock means generalized inadequate blood flow through the body, to the extent that the body tissues are damaged because of too little flow, especially because of too little oxygen and other nutrients delivered to the tissue cells. Even the cardiovascular system itself—the heart musculature, walls of the blood vessels, vasomotor system, and other circulatory parts—begins to deteriorate, so that the shock, once begun, is prone to become progressively worse.

Physiologic Causes of Shock

Circulatory Shock Caused by Decreased Cardiac Output

Shock usually results from inadequate cardiac output. Therefore, any condition that reduces the cardiac output far below normal will likely lead to circulatory shock. Two types of factors can severely reduce cardiac output:

1. *Cardiac abnormalities that decrease the ability of the heart to pump blood.* These include especially *myocardial infarction* but also *toxic states* of the heart, *severe heart valve dysfunction,* heart *arrhythmias,* and other conditions. The circulatory shock that results from diminished cardiac pumping ability is called *cardiogenic shock.* This is discussed in detail in Chapter 22, where it is pointed out that as many as 85 per cent of people who develop cardiogenic shock do not survive.
2. *Factors that decrease venous return* also decrease cardiac output because the heart cannot pump blood that does not flow into it. The most common cause of decreased venous return is *diminished blood volume,* but venous return can also be reduced as a result of *decreased vascular tone,* especially of the venous blood reservoirs, or *obstruction to blood flow* at some point in the circulation, especially in the venous return pathway to the heart.

Circulatory Shock That Occurs Without Diminished Cardiac Output

Occasionally, the cardiac output is normal or even greater than normal, yet the person is in circulatory shock. This can result from (1) *excessive metabolism of the body, so that even a normal cardiac output is inadequate,* or (2) *abnormal tissue perfusion patterns, so that most of the cardiac output is passing through blood vessels besides those that supply the local tissues with nutrition.*

The specific causes of shock are discussed later in the chapter. For the present, it is important to note that all of them lead to *inadequate delivery of nutrients to critical tissues and critical organs and also cause inadequate removal of cellular waste products from the tissues.*

What Happens to the Arterial Pressure in Circulatory Shock?

In the minds of many physicians, the arterial pressure level is the principal measure of adequacy of circulatory function. However, the arterial pressure can often be seriously misleading. At times, a person may be in severe shock and still have an almost normal arterial pressure because of powerful nervous reflexes that keep the pressure from falling. At other times, the arterial pressure can fall to half of normal, but the person still has normal tissue perfusion and is not in shock.

In most types of shock, especially shock caused by severe blood loss, the arterial blood pressure decreases at the same time as the cardiac output decreases, although usually not as much.

Tissue Deterioration Is the End Result of Circulatory Shock, Whatever the Cause

Once circulatory shock reaches a critical state of severity, regardless of its initiating cause, *the shock itself breeds more shock.* That is, the inadequate blood flow causes the body tissues to begin deteriorating, including the heart and circulatory system itself. This causes an even greater decrease in cardiac output, and a vicious circle ensues, with progressively increasing circulatory shock, less adequate tissue perfusion, more shock, and so forth until death. It is with this late stage of circulatory shock that we are especially concerned, because appropriate physiologic treatment can often reverse the rapid slide to death.

Stages of Shock

Because the characteristics of circulatory shock change with different degrees of severity, shock is divided into the following three major stages:

1. A *nonprogressive stage* (sometimes called the *compensated stage*), in which the normal circulatory compensatory mechanisms eventually cause full recovery without help from outside therapy.
2. A *progressive stage,* in which, without therapy, the shock becomes steadily worse until death.
3. An *irreversible stage,* in which the shock has progressed to such an extent that all forms of known therapy are inadequate to save the person's life, even though, for the moment, the person is still alive.

Now, let us discuss the stages of circulatory shock caused by decreased blood volume, which illustrate the basic principles. Then we can consider special characteristics of shock initiated by other causes.

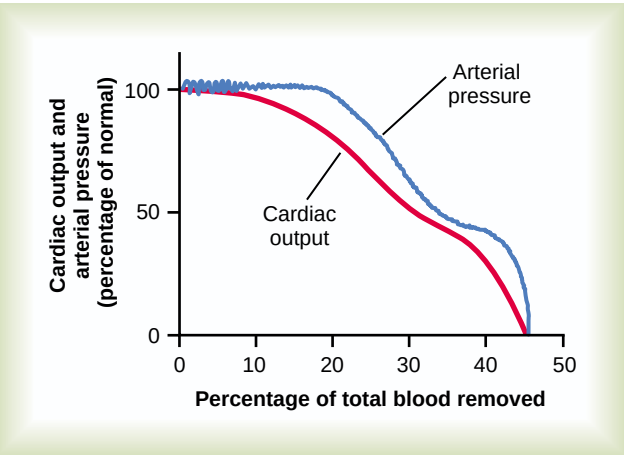


Figure 24–1

Effect of hemorrhage on cardiac output and arterial pressure.

Shock Caused by Hypovolemia—Hemorrhagic Shock

Hypovolemia means diminished blood volume. Hemorrhage is the most common cause of hypovolemic shock. Hemorrhage *decreases the filling pressure of the circulation* and, as a consequence, decreases venous return. As a result, the cardiac output falls below normal, and shock may ensue.

Relationship of Bleeding Volume to Cardiac Output and Arterial Pressure

Figure 24–1 shows the approximate effects on both cardiac output and arterial pressure of removing blood from the circulatory system over a period of about 30 minutes. About 10 per cent of the total blood volume can be removed with almost no effect on either arterial pressure or cardiac output, but greater blood loss usually diminishes the cardiac output first and later the arterial pressure, both of which fall to zero when about 35 to 45 per cent of the total blood volume has been removed.

Sympathetic Reflex Compensations in Shock—Their Special Value to Maintain Arterial Pressure. The decrease in arterial pressure after hemorrhage—as well as decreases in pressures in the pulmonary arteries and veins in the thorax—causes powerful sympathetic reflexes (initiated mainly by the arterial baroreceptors and other vascular stretch receptors, as explained in Chapter 18). These reflexes stimulate the sympathetic vasoconstrictor system throughout the body, resulting in three important effects: (1) The arterioles constrict in most parts of the systemic circulation, thereby increasing the total peripheral resistance. (2) The veins and venous reservoirs constrict, thereby helping to maintain adequate venous return despite diminished blood

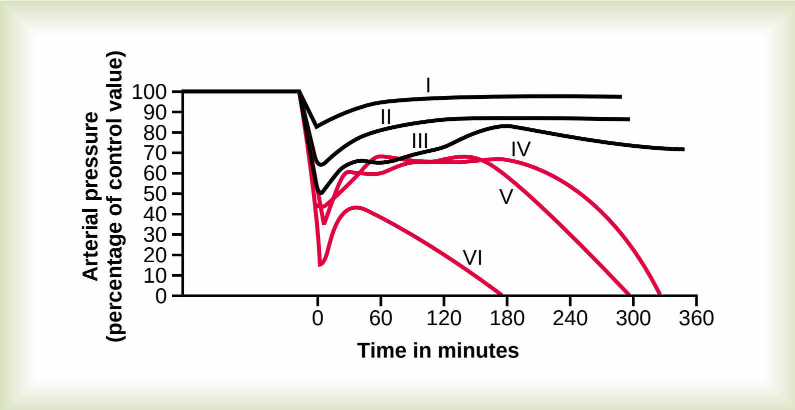


Figure 24–2

Time course of arterial pressure in dogs after different degrees of acute hemorrhage. Each curve represents average results from six dogs.

volume. (3) Heart activity increases markedly, sometimes increasing the heart rate from the normal value of 72 beats/min to as high as 160 to 180 beats/min.

Value of the Sympathetic Nervous Reflexes. In the absence of the sympathetic reflexes, only 15 to 20 per cent of the blood volume can be removed over a period of 30 minutes before a person dies; this is in contrast to a 30 to 40 per cent loss of blood volume that a person can sustain when the reflexes are intact. Therefore, the reflexes extend the amount of blood loss that can occur without causing death to about twice that which is possible in their absence.

Greater Effect of the Sympathetic Nervous Reflexes in Maintaining Arterial Pressure than in Maintaining Cardiac Output. Referring again to Figure 24–1, note that the arterial pressure is maintained at or near normal levels in the hemorrhaging person longer than is the cardiac output. The reason for this is that the sympathetic reflexes are geared more for maintaining arterial pressure than for maintaining output. They increase the arterial pressure mainly by increasing the total peripheral resistance, which has no beneficial effect on cardiac output; however, the *sympathetic constriction of the veins is important to keep venous return and cardiac output from falling too much*, in addition to their role in maintaining arterial pressure.

Especially interesting is the second plateau occurring at about 50 mm Hg in the arterial pressure curve of Figure 24–1. This results from activation of the central nervous system ischemic response, which causes extreme stimulation of the sympathetic nervous system when the brain begins to suffer from lack of oxygen or from excess buildup of carbon dioxide, as discussed in Chapter 18. This effect of the central nervous system ischemic response can be called the "last-ditch stand" of the sympathetic reflexes in their attempt to keep the arterial pressure from falling too low.

Protection of Coronary and Cerebral Blood Flow by the Reflexes. A special value of the maintenance of normal arterial pressure even in the presence of decreasing cardiac output is protection of blood flow through the coronary and cerebral circulatory systems. The sympathetic stimulation does not cause significant constriction of either the cerebral or the cardiac vessels. In addition, in both these vascular beds, local blood flow autoregulation is excellent, which prevents moderate decreases in arterial pressure from significantly decreasing their blood flows. Therefore, blood flow through the heart and brain is maintained essentially at normal levels as long as the arterial pressure does not fall below about 70 mm Hg, despite the fact that blood flow in some other areas of the body might be decreased to as little as one third to one quarter normal by this time because of vasoconstriction.

Progressive and Nonprogressive Hemorrhagic Shock

Figure 24–2 shows an experiment that we performed in dogs to demonstrate the effects of different degrees of sudden acute hemorrhage on the subsequent course of arterial pressure. The dogs were bled rapidly until their arterial pressures fell to different levels. Those dogs whose pressures fell immediately to no lower than 45 mm Hg (groups I, II, and III) all eventually recovered; the recovery occurred rapidly if the pressure fell only slightly (group I) but occurred slowly if it fell almost to the 45 mm Hg level (group III). When the arterial pressure fell below 45 mm Hg (groups IV, V, and VI), all the dogs died, although many of them hovered between life and death for hours before the circulatory system deteriorated to the stage of death.

This experiment demonstrates that the circulatory system can recover as long as the degree of hemorrhage is no greater than a certain critical amount. Crossing this critical threshold by even a few milliliters of blood loss makes the eventual difference between life and death. Thus, hemorrhage beyond a certain critical level causes shock to become *progressive*. That is, *the shock itself causes still more shock*, and the condition becomes a vicious circle that eventually leads to deterioration of the circulation and to death.

Nonprogressive Shock—Compensated Shock

If shock is not severe enough to cause its own progression, the person eventually recovers. Therefore, shock of this lesser degree is called *nonprogressive*

shock. It is also called *compensated shock,* meaning that the sympathetic reflexes and other factors compensate enough to prevent further deterioration of the circulation.

The factors that cause a person to recover from moderate degrees of shock are all the negative feedback control mechanisms of the circulation that attempt to return cardiac output and arterial pressure back to normal levels. They include the following:

1. *Baroreceptor reflexes,* which elicit powerful sympathetic stimulation of the circulation.
2. *Central nervous system ischemic response,* which elicits even more powerful sympathetic stimulation throughout the body but is not activated significantly until the arterial pressure falls below 50 mm Hg.
3. *Reverse stress-relaxation of the circulatory system,* which causes the blood vessels to contract around the diminished blood volume, so that the blood volume that is available more adequately fills the circulation.
4. *Formation of angiotensin by the kidneys,* which constricts the peripheral arteries and also causes decreased output of water and salt by the kidneys, both of which help prevent progression of shock.
5. *Formation of vasopressin (antidiuretic hormone) by the posterior pituitary gland,* which constricts the peripheral arteries and veins and greatly increases water retention by the kidneys.
6. *Compensatory mechanisms that return the blood volume back toward normal,* including absorption of large quantities of fluid from the intestinal tract, absorption of fluid into the blood capillaries from the interstitial spaces of the body, conservation of water and salt by the kidneys, and increased thirst and increased appetite for salt, which make the person drink water and eat salty foods if able.

The sympathetic reflexes provide immediate help toward bringing about recovery because they become maximally activated within 30 seconds to a minute after hemorrhage.

The angiotensin and vasopressin mechanisms, as well as the reverse stress-relaxation that causes contraction of the blood vessels and venous reservoirs, all require 10 minutes to 1 hour to respond completely, but they aid greatly in increasing the arterial pressure or increasing the circulatory filling pressure and thereby increasing the return of blood to the heart.

Finally, readjustment of blood volume by absorption of fluid from the interstitial spaces and intestinal tract, as well as oral ingestion and absorption of additional quantities of water and salt, may require from 1 to 48 hours, but recovery eventually takes place, provided the shock does not become severe enough to enter the progressive stage.

"Progressive Shock" Is Caused by a Vicious Circle of Cardiovascular Deterioration

Figure 24–3 shows some of the positive feedbacks that further depress cardiac output in shock, thus causing the shock to become progressive. Some of the more important feedbacks are the following.

Cardiac Depression. When the arterial pressure falls low enough, *coronary blood flow decreases below that required for adequate nutrition of the myocardium.* This weakens the heart muscle and thereby decreases the cardiac output more. Thus, a positive feedback cycle has developed, whereby the shock becomes more and more severe.

Figure 24–4 shows cardiac output curves extrapolated to the human heart from experiments in dogs, demonstrating progressive deterioration of the heart at different times after the onset of shock. A dog was bled until the arterial pressure fell to 30 mm Hg, and the pressure was held at this level by further bleeding or retransfusion of blood as required. Note from the second curve in the figure that there was little deterioration of the heart during the first 2 hours, but by 4 hours, the heart had deteriorated about 40 per cent; then, rapidly, during the last hour of the experiment (after 4 hours of low coronary blood pressure), the heart deteriorated completely.

Thus, one of the important features of progressive shock, whether it is hemorrhagic in origin or caused in another way, is eventual progressive deterioration of the heart. In the early stages of shock, this plays very little role in the condition of the person, partly because deterioration of the heart is not severe during the first hour or so of shock, but mainly because the heart has tremendous reserve capability that normally allows it to pump 300 to 400 per cent more blood than is required by the body for adequate bodywide tissue nutrition. In the latest stages of shock, however, deterioration of the heart is probably the most important factor in the final lethal progression of the shock.

Vasomotor Failure. In the early stages of shock, various circulatory reflexes cause intense activity of the sympathetic nervous system. This, as discussed earlier, helps delay depression of the cardiac output and especially helps prevent decreased arterial pressure. However, there comes a point when diminished blood flow to the brain's vasomotor center depresses the center so much that it, too, becomes progressively less active and finally totally inactive. For instance, *complete circulatory arrest to the brain* causes, during the first 4 to 8 minutes, the most intense of all sympathetic discharges, but by the end of 10 to 15 minutes, the vasomotor center becomes so depressed that no further evidence of sympathetic discharge can be demonstrated. Fortunately, the vasomotor center usually does not fail in the early stages of shock if the arterial pressure remains above 30 mm Hg.

Blockage of Very Small Vessels—"Sludged Blood." In time, blockage occurs in many of the very small blood vessels in the circulatory system, and this also causes the shock to progress. The initiating cause of this blockage is sluggish blood flow in the microvessels. Because tissue metabolism continues despite the low flow, large amounts of acid, both carbonic acid and

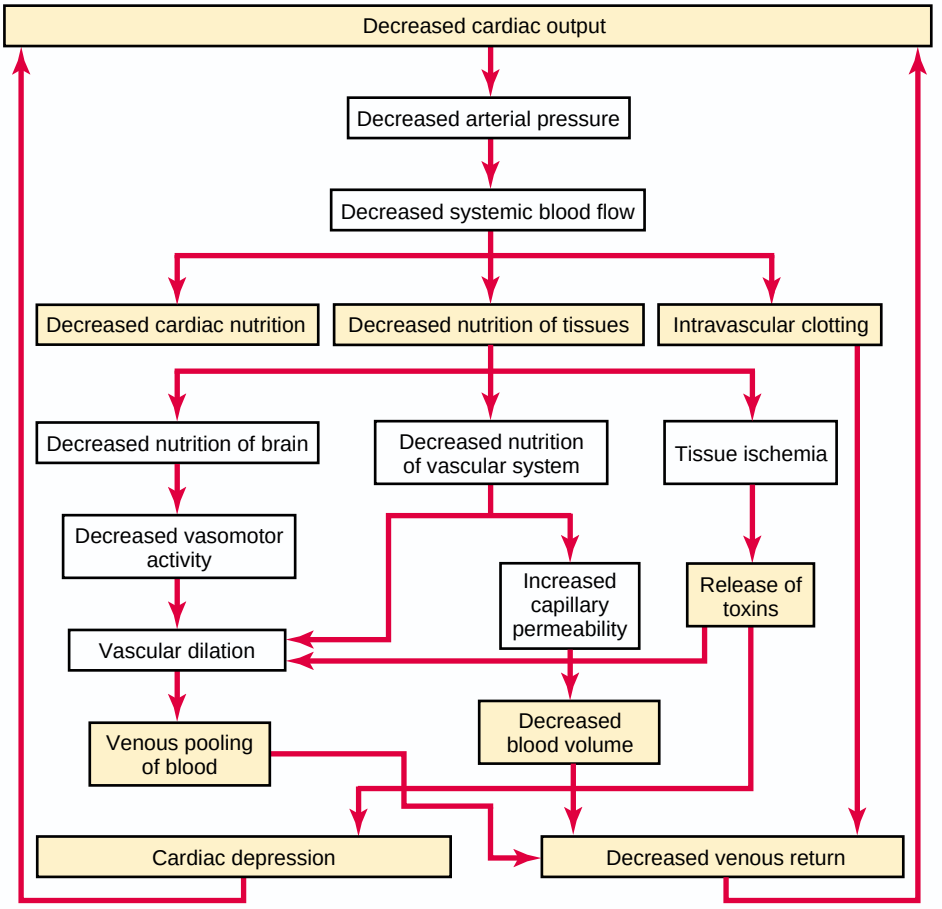


Figure 24–3

Different types of "positive feedback" that can lead to progression of shock.

lactic acid, continue to empty into the local blood vessels and greatly increase the local acidity of the blood. This acid, plus other deterioration products from the ischemic tissues, causes local blood agglutination, resulting in minute blood clots, leading to very small plugs in the small vessels. Even if the vessels do not become plugged, an increased tendency for the blood cells to stick to one another makes it more difficult for blood to flow through the microvasculature, giving rise to the term *sludged blood.*

Increased Capillary Permeability. After many hours of capillary hypoxia and lack of other nutrients, the permeability of the capillaries gradually increases, and large quantities of fluid begin to transude into the tissues. This decreases the blood volume even more, with a resultant further decrease in cardiac output, making the shock still more severe. Capillary hypoxia does not cause increased capillary permeability until the late stages of prolonged shock.

Release of Toxins by Ischemic Tissue. Throughout the history of research in the field of shock, it has been suggested that shock causes tissues to release toxic substances, such as histamine, serotonin, and tissue enzymes, that cause further deterioration of the circulatory system. Quantitative studies have proved the significance of at least one toxin, *endotoxin,* in some types of shock.

Cardiac Depression Caused by Endotoxin. *Endotoxin* is released from the bodies of dead gram-negative bacteria in the intestines. Diminished blood flow to the intestines often causes enhanced formation and absorption of this toxic substance. The circulating toxin then causes increased cellular metabolism despite inadequate nutrition of the cells; this has a specific effect on the heart muscle, causing *cardiac depression.* Endotoxin can play a major role in some types of shock, especially "septic shock," discussed later in the chapter.

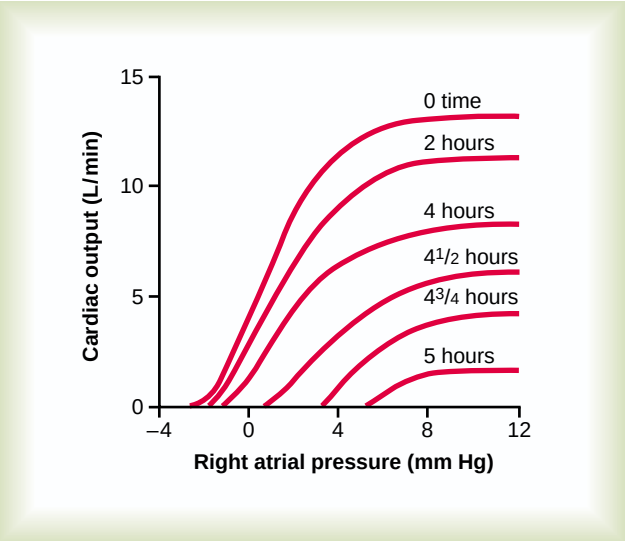


Figure 24–4

Cardiac output curves of the heart at different times after hemorrhagic shock begins. (These curves are extrapolated to the human heart from data obtained in dog experiments by Dr. J. W. Crowell.)

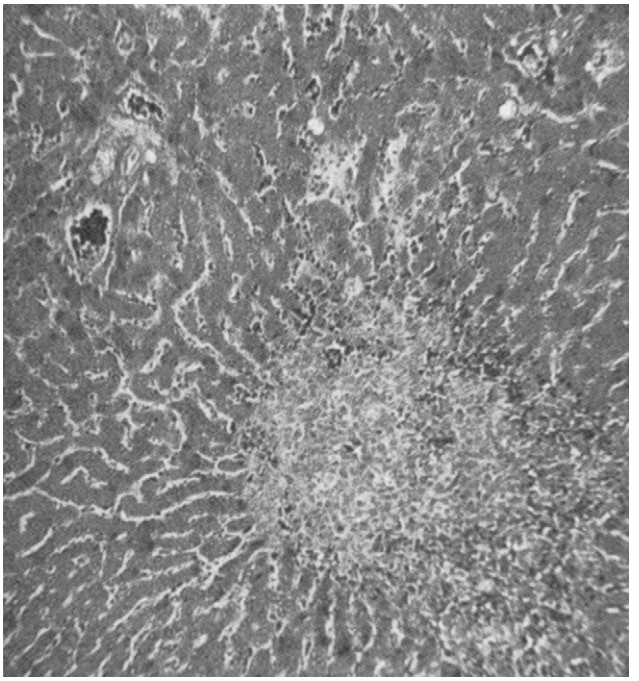


Figure 24–5

Necrosis of the central portion of a liver lobule in severe circulatory shock. (Courtesy Dr. J. W. Crowell.)

Generalized Cellular Deterioration. As shock becomes severe, many signs of generalized cellular deterioration occur throughout the body. One organ especially affected is the *liver,* as illustrated in Figure 24–5. This occurs mainly because of lack of enough nutrients to support the normally high rate of metabolism in liver cells, but also partly because of the extreme exposure of the liver cells to any vascular toxin or other abnormal metabolic factor occurring in shock.

Among the damaging cellular effects that are known to occur in most body tissues are the following:

1. Active transport of sodium and potassium through the cell membrane is greatly diminished. As a result, sodium and chloride accumulate in the cells, and potassium is lost from the cells. In addition, the cells begin to swell.
2. Mitochondrial activity in the liver cells, as well as in many other tissues of the body, becomes severely depressed.
3. Lysosomes in the cells in widespread tissue areas begin to break open, with intracellular release of *hydrolases* that cause further intracellular deterioration.
4. Cellular metabolism of nutrients, such as glucose, eventually becomes greatly depressed in the last stages of shock. The actions of some hormones are depressed as well, including almost 100 per cent depression of the action of insulin.

All these effects contribute to further deterioration of many organs of the body, including especially (1) the *liver,* with depression of its many metabolic and detoxification functions; (2) the *lungs,* with eventual development of pulmonary edema and poor ability to oxygenate the blood; and (3) the *heart,* thereby further depressing its contractility.

Tissue Necrosis in Severe Shock—Patchy Areas of Necrosis Occur Because of Patchy Blood Flows in Different Organs. Not all cells of the body are equally damaged by shock, because some tissues have better blood supplies than others. For instance, the cells adjacent to the arterial ends of capillaries receive better nutrition than cells adjacent to the venous ends of the same capillaries. Therefore, one would expect more nutritive deficiency around the venous ends of capillaries than elsewhere. This is precisely the effect that Crowell discovered in studying tissue areas in many parts of the body. For instance, Figure 24–5 shows necrosis in the center of a liver lobule, the portion of the lobule that is last to be exposed to the blood as it passes through the liver sinusoids.

Similar punctate lesions occur in heart muscle, although here a definite repetitive pattern, such as occurs in the liver, cannot be demonstrated. Nevertheless, the cardiac lesions play an important role in leading to the final irreversible stage of shock. Deteriorative lesions also occur in the kidneys, especially in the epithelium of the kidney tubules, leading to kidney failure and occasionally uremic death several days later. Deterioration of the lungs also often leads to respiratory distress and death several days later—called the *shock lung syndrome.*

Acidosis in Shock. Most metabolic derangements that occur in shocked tissue can lead to blood acidosis all through the body. This results from poor delivery of oxygen to the tissues, which greatly diminishes oxidative metabolism of the foodstuffs. When this occurs, the cells obtain most of their energy by the anaerobic

process of glycolysis, which leads to tremendous quantities of *excess lactic acid* in the blood. In addition, poor blood flow through tissues prevents normal removal of carbon dioxide. The carbon dioxide reacts locally in the cells with water to form high concentrations of intracellular carbonic acid; this, in turn, reacts with various tissue chemicals to form still other intracellular acidic substances. Thus, another deteriorative effect of shock is both generalized and local tissue acidosis, leading to further progression of the shock itself.

Positive Feedback Deterioration of Tissues in Shock and the Vicious Circle of Progressive Shock

All the factors just discussed that can lead to further progression of shock are types of *positive feedback*. That is, each increase in the degree of shock causes a further increase in the shock.

However, positive feedback does not necessarily lead to a vicious circle. Whether a vicious circle develops depends on the intensity of the positive feedback. In mild degrees of shock, the negative feedback mechanisms of the circulation—sympathetic reflexes, reverse stress-relaxation mechanism of the blood reservoirs, absorption of fluid into the blood from the interstitial spaces, and others—can easily overcome the positive feedback influences and, therefore, cause recovery. But in severe degrees of shock, the deteriorative feedback mechanisms become more and more powerful, leading to such rapid deterioration of the circulation that all the normal negative feedback systems of circulatory control acting together cannot return the cardiac output to normal.

Considering once again the principles of positive feedback and vicious circle discussed in Chapter 1, one can readily understand why there is a critical cardiac output level above which a person in shock recovers and below which a person enters a vicious circle of circulatory deterioration that proceeds until death.

Irreversible Shock

After shock has progressed to a certain stage, transfusion or any other type of therapy becomes incapable of saving the person's life. The person is then said to be in the *irreversible stage of shock*. Ironically, even in this irreversible stage, therapy can, on rare occasions, return the arterial pressure and even the cardiac output to normal or near normal for short periods, but the circulatory system nevertheless continues to deteriorate, and death ensues in another few minutes to few hours.

Figure 24–6 demonstrates this effect, showing that transfusion during the irreversible stage can sometimes cause the cardiac output (as well as the arterial pressure) to return to normal. However, the cardiac output soon begins to fall again, and subsequent transfusions have less and less effect. By this time, multiple deteriorative changes have occurred in the muscle cells of the heart that may not necessarily affect

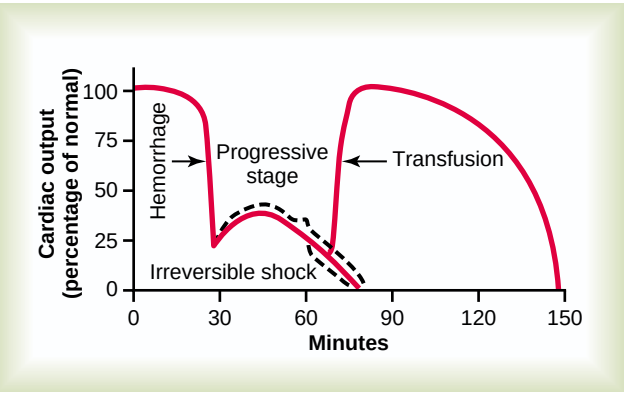


Figure 24–6

Failure of transfusion to prevent death in irreversible shock.

the heart's *immediate* ability to pump blood but, over a long period, depress heart pumping enough to cause death. Beyond a certain point, so much tissue damage has occurred, so many destructive enzymes have been released into the body fluids, so much acidosis has developed, and so many other destructive factors are now in progress that even a normal cardiac output for a few minutes cannot reverse the continuing deterioration. Therefore, in severe shock, a stage is eventually reached at which the person will die even though vigorous therapy might still return the cardiac output to normal for short periods.

Depletion of Cellular High-Energy Phosphate Reserves in Irreversible Shock. The high-energy phosphate reserves in the tissues of the body, especially in the liver and the heart, are greatly diminished in severe degrees of shock. Essentially all the *creatine phosphate* has been degraded, and almost all the *adenosine triphosphate* has downgraded to *adenosine diphosphate, adenosine monophosphate,* and, eventually, *adenosine*. Then much of this adenosine diffuses out of the cells into the circulating blood and is converted into uric acid, a substance that cannot re-enter the cells to reconstitute the adenosine phosphate system. New adenosine can be synthesized at a rate of only about 2 per cent of the normal cellular amount an hour, meaning that once the high-energy phosphate stores of the cells are depleted, they are difficult to replenish.

Thus, one of the most devastating end results of deterioration in shock, and the one that is perhaps most significant for development of the final state of irreversibility, is this cellular depletion of these high-energy compounds.

Hypovolemic Shock Caused by Plasma Loss

Loss of plasma from the circulatory system, even without loss of red blood cells, can sometimes be severe enough to reduce the total blood volume

markedly, causing typical hypovolemic shock similar in almost all details to that caused by hemorrhage. Severe plasma loss occurs in the following conditions:

1. *Intestinal obstruction* is often a cause of severely reduced plasma volume. Distention of the intestine in intestinal obstruction partly blocks venous blood flow in the intestinal walls, which increases intestinal capillary pressure. This in turn causes fluid to leak from the capillaries into the intestinal walls and also into the intestinal lumen. Because the lost fluid has a high protein content, the result is reduced total blood plasma protein as well as reduced plasma volume.
2. In almost all patients who have *severe burns* or other denuding conditions of the skin, so much plasma is lost through the denuded skin areas that the plasma volume becomes markedly reduced.

The hypovolemic shock that results from plasma loss has almost the same characteristics as the shock caused by hemorrhage, except for one additional complicating factor: the blood viscosity increases greatly as a result of increased red blood cell concentration in the remaining blood, and this exacerbates the sluggishness of blood flow.

Loss of fluid from all fluid compartments of the body is called *dehydration;* this, too, can reduce the blood volume and cause hypovolemic shock similar to that resulting from hemorrhage. Some of the causes of this type of shock are (1) excessive sweating, (2) fluid loss in severe diarrhea or vomiting, (3) excess loss of fluid by nephrotic kidneys, (4) inadequate intake of fluid and electrolytes, or (5) destruction of the adrenal cortices, with loss of aldosterone secretion and consequent failure of the kidneys to reabsorb sodium, chloride, and water, which occurs in the absence of the adrenocortical hormone aldosterone.

Hypovolemic Shock Caused by Trauma

One of the most common causes of circulatory shock is trauma to the body. Often the shock results simply from hemorrhage caused by the trauma, but it can also occur even without hemorrhage, because extensive contusion of the body can damage the capillaries sufficiently to allow excessive loss of plasma into the tissues. This results in greatly reduced plasma volume, with resultant hypovolemic shock.

Various attempts have been made to implicate toxic factors released by the traumatized tissues as one of the causes of shock after trauma. However, cross-transfusion experiments into normal animals have failed to show significant toxic elements.

In summary, traumatic shock seems to result mainly from hypovolemia, although there might also be a moderate degree of concomitant neurogenic shock caused by loss of vasomotor tone, as discussed next.

Neurogenic Shock—Increased Vascular Capacity

Shock occasionally results without any loss of blood volume. Instead, the *vascular capacity* increases so much that even the normal amount of blood becomes incapable of filling the circulatory system adequately. One of the major causes of this is *sudden loss of vasomotor tone* throughout the body, resulting especially in massive dilation of the veins. The resulting condition is known as *neurogenic shock.*

The role of vascular capacity in helping to regulate circulatory function was discussed in Chapter 15, where it was pointed out that either an increase in vascular capacity or a decrease in blood volume *reduces the mean systemic filling pressure,* which reduces venous return to the heart. Diminished venous return caused by vascular dilation is called *venous pooling* of blood.

Causes of Neurogenic Shock. Some neurogenic factors that can cause loss of vasomotor tone include the following:

1. *Deep general anesthesia* often depresses the vasomotor center enough to cause vasomotor paralysis, with resulting neurogenic shock.
2. *Spinal anesthesia,* especially when this extends all the way up the spinal cord, blocks the sympathetic nervous outflow from the nervous system and can be a potent cause of neurogenic shock.
3. *Brain damage* is often a cause of vasomotor paralysis. Many patients who have had brain concussion or contusion of the basal regions of the brain develop profound neurogenic shock. Also, even though brain ischemia for a few minutes almost always causes extreme vasomotor stimulation, prolonged ischemia (lasting longer than 5 to 10 minutes) can cause the opposite effect—total inactivation of the vasomotor neurons in the brain stem, with consequent development of severe neurogenic shock.

Anaphylactic Shock and Histamine Shock

Anaphylaxis is an allergic condition in which the cardiac output and arterial pressure often decrease drastically. This is discussed in Chapter 34. It results primarily from an antigen-antibody reaction that takes place immediately after an antigen to which the person is sensitive enters the circulation. One of the principal effects is to cause the *basophils* in the blood and *mast* cells in the pericapillary tissues to release *histamine* or a *histamine-like substance.* The histamine causes (1) an increase in vascular capacity because of venous dilation, thus causing a marked decrease in venous return; (2) dilation of the arterioles, resulting in greatly reduced arterial pressure; and (3) greatly increased capillary permeability, with rapid loss of fluid and

protein into the tissue spaces. The net effect is a great reduction in venous return and sometimes such serious shock that the person dies within minutes.

Intravenous injection of large amounts of histamine causes "histamine shock," which has characteristics almost identical to those of anaphylactic shock.

Septic Shock

A condition that was formerly known by the popular name "blood poisoning" is now called *septic shock* by most clinicians. This refers to a bacterial infection widely disseminated to many areas of the body, with the infection being borne through the blood from one tissue to another and causing extensive damage. There are many varieties of septic shock because of the many types of bacterial infections that can cause it and because infection in different parts of the body produces different effects.

Septic shock is extremely important to the clinician, because other than cardiogenic shock, septic shock is the most frequent cause of shock-related death in the modern hospital.

Some of the typical causes of septic shock include the following:

1. Peritonitis caused by spread of infection from the uterus and fallopian tubes, sometimes resulting from instrumental abortion performed under unsterile conditions.
2. Peritonitis resulting from rupture of the gastrointestinal system, sometimes caused by intestinal disease and sometimes by wounds.
3. Generalized bodily infection resulting from spread of a skin infection such as streptococcal or staphylococcal infection.
4. Generalized gangrenous infection resulting specifically from gas gangrene bacilli, spreading first through peripheral tissues and finally by way of the blood to the internal organs, especially the liver.
5. Infection spreading into the blood from the kidney or urinary tract, often caused by colon bacilli.

Special Features of Septic Shock. Because of the multiple types of septic shock, it is difficult to categorize this condition. Some features often observed are:

1. High fever.
2. Often marked vasodilation throughout the body, especially in the infected tissues.
3. High cardiac output in perhaps half of patients, caused by arteriolar dilation in the infected tissues and by high metabolic rate and vasodilation elsewhere in the body, resulting from bacterial toxin stimulation of cellular metabolism and from high body temperature.
4. Sludging of the blood, caused by red cell agglutination in response to degenerating tissues.
5. Development of micro–blood clots in widespread areas of the body, a condition called *disseminated intravascular coagulation.* Also, this causes the blood clotting factors to be used up, so that hemorrhaging occurs in many tissues, especially in the gut wall of the intestinal tract.

In early stages of septic shock, the patient usually does not have signs of circulatory collapse but only signs of the bacterial infection. As the infection becomes more severe, the circulatory system usually becomes involved either because of direct extension of the infection or secondarily as a result of toxins from the bacteria, with resultant loss of plasma into the infected tissues through deteriorating blood capillary walls. There finally comes a point at which deterioration of the circulation becomes progressive in the same way that progression occurs in all other types of shock. The end stages of septic shock are not greatly different from the end stages of hemorrhagic shock, even though the initiating factors are markedly different in the two conditions.

Physiology of Treatment in Shock

Replacement Therapy

Blood and Plasma Transfusion. If a person is in shock caused by hemorrhage, the best possible therapy is usually transfusion of whole blood. If the shock is caused by plasma loss, the best therapy is administration of plasma; when dehydration is the cause, administration of an appropriate electrolyte solution can correct the shock.

Whole blood is not always available, such as under battlefield conditions. Plasma can usually substitute adequately for whole blood because it increases the blood volume and restores normal hemodynamics. Plasma cannot restore a normal hematocrit, but the human body can usually stand a decrease in hematocrit to about half of normal before serious consequences result, if cardiac output is adequate. Therefore, in emergency conditions, it is reasonable to use plasma in place of whole blood for treatment of hemorrhagic or most other types of hypovolemic shock.

Sometimes plasma is unavailable. In these instances, various *plasma substitutes* have been developed that perform almost exactly the same hemodynamic functions as plasma. One of these is dextran solution.

Dextran Solution as a Plasma Substitute. The principal requirement of a truly effective plasma substitute is that it remain in the circulatory system—that is, not filter through the capillary pores into the tissue spaces. In addition, the solution must be nontoxic and must contain appropriate electrolytes to prevent derangement of the body's extracellular fluid electrolytes on administration.

To remain in the circulation, the plasma substitute must contain some substance that has a large enough molecular size to exert colloid osmotic pressure. One of the most satisfactory substances developed for this

purpose is *dextran,* a large polysaccharide polymer of glucose. Certain bacteria secrete dextran as a by-product of their growth, and commercial dextran can be manufactured using a bacterial culture procedure. By varying the growth conditions of the bacteria, the molecular weight of the dextran can be controlled to the desired value. Dextrans of appropriate molecular size do not pass through the capillary pores and, therefore, can replace plasma proteins as colloid osmotic agents.

Few toxic reactions have been observed when using purified dextran to provide colloid osmotic pressure; therefore, solutions containing this substance have proved to be a satisfactory substitute for plasma in most fluid replacement therapy.

Treatment of Shock with Sympathomimetic Drugs—Sometimes Useful, Sometimes Not

A *sympathomimetic drug* is a drug that mimics sympathetic stimulation. These drugs include *norepinephrine*, *epinephrine*, and a large number of long-acting drugs that have the same effect as epinephrine and norepinephrine.

In two types of shock, sympathomimetic drugs have proved to be especially beneficial. The first of these is *neurogenic shock,* in which the sympathetic nervous system is severely depressed. Administering a sympathomimetic drug takes the place of the diminished sympathetic actions and can often restore full circulatory function.

The second type of shock in which sympathomimetic drugs are valuable is *anaphylactic shock,* in which excess histamine plays a prominent role. The sympathomimetic drugs have a vasoconstrictor effect that opposes the vasodilating effect of histamine. Therefore, either norepinephrine or another sympathomimetic drug is often lifesaving.

Sympathomimetic drugs have not proved to be very valuable in hemorrhagic shock. The reason is that in this type of shock, the sympathetic nervous system is almost always maximally activated by the circulatory reflexes already; so much norepinephrine and epinephrine are already circulating in the blood that sympathomimetic drugs have essentially no additional beneficial effect.

Other Therapy

Treatment by the Head-Down Position. When the pressure falls too low in most types of shock, especially in hemorrhagic and neurogenic shock, placing the patient with the head at least 12 inches lower than the feet helps tremendously in promoting venous return, thereby also increasing cardiac output. This head-down position is the first essential step in the treatment of many types of shock.

Oxygen Therapy. Because the major deleterious effect of most types of shock is too little delivery of oxygen to the tissues, giving the patient oxygen to breathe can be of benefit in many instances. However, this frequently is far less beneficial than one might expect, because the problem in most types of shock is not inadequate oxygenation of the blood by the lungs but inadequate transport of the blood after it is oxygenated.

Treatment with Glucocorticoids (Adrenal Cortex Hormones That Control Glucose Metabolism). Glucocorticoids are frequently given to patients in severe shock for several reasons: (1) experiments have shown empirically that glucocorticoids frequently increase the strength of the heart in the late stages of shock; (2) glucocorticoids stabilize lysosomes in tissue cells and thereby prevent release of lysosomal enzymes into the cytoplasm of the cells, thus preventing deterioration from this source; and (3) glucocorticoids might aid in the metabolism of glucose by the severely damaged cells.

Circulatory Arrest

A condition closely allied to circulatory shock is circulatory arrest, in which all blood flow stops. This occurs frequently on the surgical operating table as a result of *cardiac arrest* or *ventricular fibrillation.*

Ventricular fibrillation can usually be stopped by strong electroshock of the heart, the basic principles of which are described in Chapter 13.

Cardiac arrest often results from too little oxygen in the anesthetic gaseous mixture or from a depressant effect of the anesthesia itself. A normal cardiac rhythm can usually be restored by removing the anesthetic and immediately applying cardiopulmonary resuscitation procedures, while at the same time supplying the patient's lungs with adequate quantities of ventilatory oxygen.

Effect of Circulatory Arrest on the Brain

A special problem in circulatory arrest is to prevent detrimental effects in the brain as a result of the arrest. In general, more than 5 to 8 minutes of total circulatory arrest can cause at least some degree of permanent brain damage in more than half of patients. Circulatory arrest for as long as 10 to 15 minutes almost always permanently destroys significant amounts of mental power.

For many years, it was taught that this detrimental effect on the brain was caused by the acute cerebral hypoxia that occurs during circulatory arrest. However, experiments have shown that if blood clots are prevented from occurring in the blood vessels of the brain, this will also prevent most of the early deterioration of the brain during circulatory arrest. For instance, in animal experiments performed by Crowell, all the blood was removed from the animal's blood vessels at the beginning of circulatory arrest and then replaced at the end of circulatory arrest so that no intravascular blood clotting could occur. In this

experiment, the brain was usually able to withstand up to 30 minutes of circulatory arrest without permanent brain damage. Also, administration of heparin or streptokinase (to prevent blood coagulation) before cardiac arrest was shown to increase the survivability of the brain up to two to four times longer than usual.

It is likely that the severe brain damage that occurs from circulatory arrest is caused mainly by permanent blockage of many small blood vessels by blood clots, thus leading to prolonged ischemia and eventual death of the neurons.

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