- *Hypoxemia.* Understandably, abnormally low blood O_2 content (regardless of cause) increases both the likelihood and extent of infarction.

KEY CONCEPTS

Infarction

- Infarcts are areas of ischemic necrosis most commonly caused by arterial occlusion (typically due to thrombosis or embolization); venous outflow obstruction is a less frequent cause.
- Infarcts caused by venous occlusion or occurring in spongy tissues with dual blood supply and where blood can collect typically are hemorrhagic (red); those caused by arterial occlusion in compact tissues typically are pale (white).
- Whether or not vascular occlusion causes tissue infarction is influenced by collateral blood supplies, the rate at which an obstruction develops, intrinsic tissue susceptibility to ischemic injury, and blood oxygenation.

Shock

Shock is a state in which diminished cardiac output or reduced effective circulating blood volume impairs tissue perfusion and leads to cellular hypoxia. At the outset the cellular injury is reversible; however, prolonged shock eventually leads to irreversible tissue injury and is often fatal. Shock may complicate severe hemorrhage, extensive trauma or burns, myocardial infarction, pulmonary embolism, and microbial sepsis. Its causes fall into three general categories (Table 4-3):

- *Cardiogenic shock* results from low cardiac output due to myocardial pump failure. This can be due to intrinsic myocardial damage (infarction), ventricular arrhythmias, extrinsic compression (cardiac tamponade; Chapter 11), or outflow obstruction (e.g., pulmonary embolism).
- *Hypovolemic shock* results from low cardiac output due to low blood volume, such as can occur with massive hemorrhage or fluid loss from severe burns.
- *Shock associated with systemic inflammation* may be triggered by a variety of insults, particularly microbial infections, burns, trauma, and or pancreatitis. The common pathogenic feature is a massive outpouring of inflammatory mediators from innate and adaptive immune cells that produce arterial vasodilation, vascular leakage, and venous blood pooling. These cardiovascular abnormalities result in tissue hypoperfusion, cellular hypoxia, and metabolic derangements that lead to organ dysfunction and, if severe and persistent, organ failure and death. It should be noted that diverse triggers of shock (microbial and non-microbial) associated with inflammation produce a similar set of clinical findings, which are referred to as the *systemic inflammatory response syndrome*. The pathogenesis of shock caused by microbial infection *(septic shock)* is discussed in detail below.

Less commonly, shock can occur in the setting of an anesthetic accident or a spinal cord injury *(neurogenic shock)*, or an IgE–mediated hypersensitivity reaction (*anaphylactic shock*, Chapter 6). In both of these forms of shock, acute vasodilation leads to hypotension and tissue hypoperfusion.

Pathogenesis of Septic Shock

With a mortality rate exceeding 20%, septic shock ranks first among the causes of death in intensive care units and accounts for over 200,000 lost lives each year in the United States. Its incidence is rising, ironically due to improvements in life support for critically ill patients, as well as the growing ranks of immunocompromised hosts (due to chemotherapy, immunosuppression, advanced age or HIV infection) and the increasing prevalence of multidrug resistant organisms in the hospital setting. Septic shock is most frequently triggered by gram-positive bacterial infections, followed by gram-negative bacteria and fungi. Hence, an older synonym, "endotoxic shock", is no longer appropriate.

The ability of diverse microorganisms to cause septic shock is consistent with the idea that a variety of microbial constituents can trigger the process. As you will recall from Chapter 3, macrophages, neutrophils, dendritic cells, endothelial cells, and soluble components of the innate immune system (e.g., complement) recognize and are activated by several substances derived from microorganisms. Once activated, these cells and factors initiate a number of inflammatory responses that interact in a complex, incompletely understood fashion to produce septic shock and multiorgan dysfunction (Fig. 4-20).

Factors believed to play major roles in the pathophysiology of septic shock include the following:

- *Inflammatory and counter-inflammatory responses.* In sepsis, various microbial cell wall constituents engage receptors on cells of the innate immune system,

Table 4-3 Three Major Types of Shock

Type of Shock	Clinical Example	Principal Mechanisms
Cardiogenic	Myocardial infarction Ventricular rupture Arrhythmia Cardiac tamponade Pulmonary embolism	Failure of myocardial pump resulting from intrinsic myocardial damage, extrinsic compression, or obstruction to outflow
Hypovolemic	Fluid loss (e.g., hemorrhage, vomiting, diarrhea, burns, or trauma)	Inadequate blood or plasma volume
Shock associated with systemic inflammation	Overwhelming microbial infections (bacterial and fungal) Superantigens (e.g., toxic shock syndrome) Trauma, burns, pancreatitis	Activation of cytokine cascades; peripheral vasodilation and pooling of blood; endothelial activation/injury; leukocyte-induced damage, disseminated intravascular coagulation