is widespread tissue hypoxia. In the setting of persistent oxygen deficit, intracellular aerobic respiration is replaced by anaerobic glycolysis with excessive production of lactic acid. The resulting lactic acidosis lowers the tissue pH and blunts the vasomotor response; arterioles dilate, and blood begins to pool in the microcirculation. Peripheral pooling not only worsens the cardiac output, but also puts endothelial cells at risk for developing anoxic injury with subsequent disseminated intravascular coagulation. With widespread tissue hypoxia, vital organs are affected and begin to fail.

In severe cases, the process eventually enters an irreversible stage. Widespread cell injury is reflected in lysosomal enzyme leakage, further aggravating the shock state. If ischemic bowel allows intestinal flora to enter the circulation, bacteremic septic shock may be superimposed. At this point the patient may develop anuria as a result of acute tubular necrosis and renal failure (Chapter 20), and despite heroic measures the downward clinical spiral almost inevitably culminates in death.

MORPHOLOGY

The cellular and tissue changes induced by cardiogenic or hypovolemic shock are essentially those of hypoxic injury (Chapter 2); changes can manifest in any tissue although they are particularly evident in brain, heart, lungs, kidneys, adrenals, and gastrointestinal tract. The **adrenal** changes in shock are those seen in all forms of stress; essentially there is cortical cell lipid depletion. This does not reflect adrenal exhaustion but rather conversion of the relatively inactive vacuolated cells to metabolically active cells that utilize stored lipids for the synthesis of steroids. The **kidneys** typically exhibit acute tubular necrosis (Chapter 20). The **lungs** are seldom affected in pure hypovolemic shock, because they are somewhat resistant to hypoxic injury. However, when shock is caused by sepsis or trauma, **diffuse alveolar damage** (Chapter 15) may develop, the so-called shock lung**.** In septic shock, the development of disseminated intravascular coagulation leads to widespread deposition of fibrin-rich microthrombi, particularly in the brain, heart, lungs, kidney, adrenal glands, and gastrointestinal tract. The consumption of platelets and coagulation factors also often leads to the appearance of petechial hemorrhages on serosal surface and the skin.

With the exception of neuronal and myocyte ischemic loss, virtually all of these tissues may revert to normal if the individual survives. Unfortunately, most patients with irreversible changes due to severe shock die before the tissues can recover.

Clinical Consequences. The clinical manifestations of shock depend on the precipitating insult. In hypovolemic and cardiogenic shock the patient presents with hypotension; a weak, rapid pulse; tachypnea; and cool, clammy, cyanotic skin. In septic shock the skin may initially be warm and flushed because of peripheral vasodilation. The initial threat to life stems from the underlying catastrophe that precipitated the shock (e.g., myocardial infarct, severe hemorrhage, or sepsis). Rapidly, however, shock begets cardiac, cerebral, and pulmonary dysfunction, and eventually electrolyte disturbances and metabolic acidosis exacerbate the dire state of the patient further. Individuals who survive the initial complications may enter a second phase dominated by renal insufficiency and marked by a progressive fall in urine output as well as severe fluid and electrolyte imbalances. Coagulopathy frequently complicates shock, particularly when the cause is sepsis or trauma, and can have serious or even fatal consequences, particularly in patients with severe disseminated intravascular coagulation.

The prognosis varies with the origin of shock and its duration. Thus, greater than 90% of young, otherwise healthy patients with hypovolemic shock survive with appropriate management; in comparison, septic shock, or cardiogenic shock associated with extensive myocardial infarction, are associated with substantially worse mortality rates, even with state-of-the-art care.

KEY CONCEPTS

Shock

- Shock is defined as a state of systemic tissue hypoperfusion due to reduced cardiac output and/or reduced effective circulating blood volume.
- The major types of shock are cardiogenic (e.g., myocardial infarction), hypovolemic (e.g., blood loss), and shock associated with systemic inflammatory responses (e.g., in the setting of severe infections); acute spinal or brain injuries and severe hypersensitivity reactions can also cause neurogenic and anaphylactic shock, respectively
- Shock of any form can lead to hypoxic tissue injury if not corrected.
- Septic shock is caused by the host response to bacterial, viral or fungal infections; it is a systemic inflammatory condition characterized by endothelial cell activation, tissue edema, disseminated intravascular coagulation, and metabolic derangements that often lead to organ failure and death.

SUGGESTED READINGS

Fluid Dynamics

Chen H, Schrier R: Pathophysiology of volume overload in acute heart failure syndromes. *Am J Med* 119:S11, 2006. *[Older but still useful review of heart failure and fluid overload.]*

Hemostasis and Bleeding

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De Candia E: Mechanisms of platelet activation by thrombin: a short history. *Thromb Res* 129:250–6, 2012. *[Review focused on platelet activation by PARs via thrombin, but also touching on other emerging points of possible crosstalk.]*

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Renne T, Schmaier AH, Nickel KF, et al: In vivo roles of factor XII. *Blood* 120:4296–303, 2012. *[A review summarizing new insights into the still uncertain in vivo functions of factor XII in thrombosis and vascular biology.]*