molecules on endothelial cells, thereby promoting the adhesion of leukocytes, which can damage endothelial cells by releasing reactive oxygen species and preformed proteases. Widespread endothelial injury may also be produced by deposition of antigen-antibody complexes (e.g., systemic lupus erythematosus), temperature extremes (e.g., heat stroke, burns), or microorganisms (e.g., meningococci, rickettsiae). Even subtle endothelial injury can unleash procoagulant activity by enhancing membrane expression of tissue factor.

DIC is most likely to be associated with obstetric complications, malignant neoplasms, sepsis, and major trauma. The triggers in these conditions are often multiple and interrelated. For example, in bacterial infections *endotoxins* can inhibit the endothelial expression of thrombomodulin directly or indirectly by stimulating immune cells to make TNF, and can also activate factor XII. *Antigen-antibody complexes* formed in response to the infection can activate the classical complement pathway, giving rise to complement fragments that secondarily activate both platelets and granulocytes. In *massive trauma, extensive surgery,* and *severe burns,* the major trigger is the release of procoagulants such as tissue factor. In *obstetric conditions*, procoagulants derived from the placenta, dead retained fetus, or amniotic fluid may enter the circulation. *Hypoxia, acidosis, and shock*, which often coexist in very ill patients, can also cause widespread endothelial injury, and supervening infections can complicate the problems further. *Among cancers, acute promyelocytic leukemia and adenocarcinomas* of the lung, pancreas, colon, and stomach are most frequently associated with DIC.

The possible consequences of DIC are twofold (Fig. 14-27).

- *Widespread deposition of fibrin* within the microcirculation. This leads to *ischemia* of the more severely affected or more vulnerable organs and a *microangiopathic hemolytic anemia*, which results from the fragmentation of red cells as they squeeze through the narrowed microvasculature.
- Consumption of platelets and clotting factors and the activation of plasminogen, leading to a *hemorrhagic diathesis*. Plasmin not only cleaves fibrin, but it also digests factors V and VIII, thereby reducing their concentration further. In addition, fibrin degradation products resulting from fibrinolysis inhibit platelet aggregation, fibrin polymerization, and thrombin.

MORPHOLOGY

Thrombi are most often found in the brain, heart, lungs, kidneys, adrenals, spleen, and liver, in decreasing order of frequency, but any tissue can be affected. Affected kidneys may have small thrombi in the glomeruli that evoke only reactive swelling of endothelial cells or, in severe cases, microinfarcts or even **bilateral renal cortical necrosis**. Numerous fibrin thrombi may be found in alveolar capillaries, sometimes associated with pulmonary edema and fibrin exudation, creating "hyaline membranes" reminiscent of acute respiratory distress syndrome (Chapter 15). In the central nervous system, fibrin thrombi can cause microinfarcts, occasionally complicated by simultaneous hemorrhage, which can sometimes lead to variable neurologic signs and symptoms. The manifestations in the endocrine glands are of considerable interest. In meningococcemia, fibrin thrombi within the microcirculation of the adrenal cortex are the probable basis for the massive adrenal hemorrhages seen in **Waterhouse-Friderichsen syndrome** (Chapter 24). An unusual form of DIC occurs in association with giant hemangiomas (**Kasabach-Merritt syndrome**), in which thrombi form within the neoplasm because of stasis and recurrent trauma to fragile blood vessels.

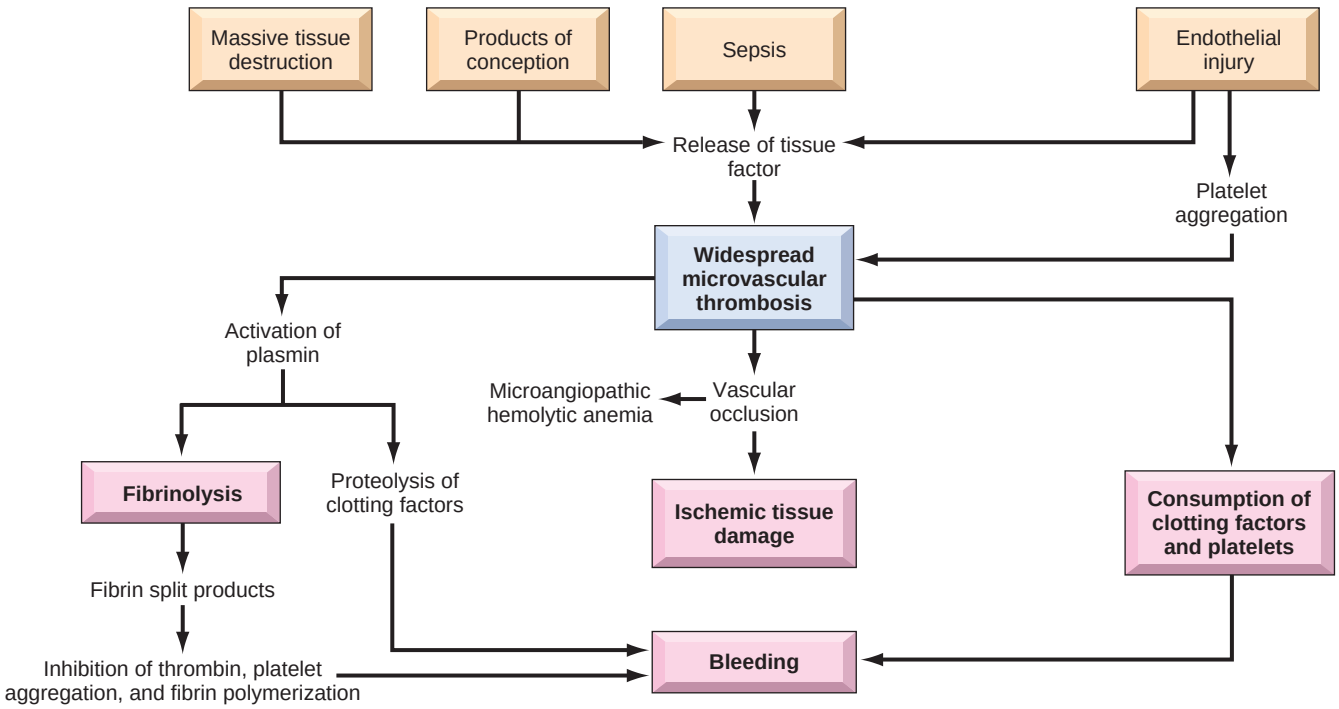

Figure 14-27 Pathophysiology of disseminated intravascular coagulation.