TABLE 141-2 COMMON CLINICAL CAUSES OF DISSEMINATED INTRAVASCULAR COAGULATION

Sepsis	Immunologic Disorders
• Bacterial: Staphylococci, streptococci, pneumococci, meningococci, gram-negative bacilli • Viral • Mycotic • Parasitic • Rickettsial	• Acute hemolytic transfusion reaction • Organ or tissue transplant rejection • Immunotherapy • Graft-versus-host disease
Trauma and Tissue Injury	**Drugs**
• Brain injury (gunshot) • Extensive burns • Fat embolism • Rhabdomyolysis	• Fibrinolytic agents • Aprotinin • Warfarin (especially in neonates with protein C deficiency) • Prothrombin complex concentrates • Recreational drugs (amphetamines)
Vascular Disorders	**Envenomation**
• Giant hemangiomas (Kasabach-Merritt syndrome) • Large vessel aneurysms (e.g., aorta)	• Snake • Insects
Obstetrical Complications	**Liver Disease**
• Abruptio placentae • Amniotic fluid embolism • Dead fetus syndrome • Septic abortion	• Fulminant hepatic failure • Cirrhosis • Fatty liver of pregnancy
Cancer	**Miscellaneous**
• Adenocarcinoma (prostate, pancreas, etc.) • Hematologic malignancies (acute promyelocytic leukemia)	• Shock • Respiratory distress syndrome • Massive transfusion

activity that overcomes the natural anticoagulant mechanisms. There are several underlying pathologies associated with DIC (Table 141-2).

The most common causes are bacterial sepsis, malignant disorders such as solid tumors or acute promyelocytic leukemia, and obstetric causes. DIC is diagnosed in almost one-half of pregnant women with abruptio placentae or with amniotic fluid embolism. Trauma, particularly to the brain, can also result in DIC. The exposure of blood to phospholipids from damaged tissue, hemolysis, and endothelial damage are all contributing factors to the development of DIC in this setting. Purpura fulminans is a severe form of DIC resulting from thrombosis of extensive areas of the skin; it affects predominantly young children following viral or bacterial infection, particularly those with inherited or acquired hypercoagulability due to deficiencies of the components of the protein C pathway. Neonates homozygous for protein C deficiency also present high risk for purpura fulminans with or without thrombosis of large vessels.

The central mechanism of DIC is the uncontrolled generation of thrombin by exposure of the blood to pathologic levels of tissue factor (Fig. 141-3). Simultaneous suppression of physiologic anticoagulant mechanisms and abnormal fibrinolysis further accelerate the process. Together, these abnormalities contribute to systemic fibrin deposition in small and midsize vessels. The duration and intensity of the fibrin deposition can compromise the blood supply of many organs, especially the lung, kidney, liver, and brain, with consequent organ failure. The sustained activation of coagulation results in consumption of clotting factors and platelets, which in turn leads to systemic bleeding. This is further aggravated by secondary hyperfibrinolysis. Studies in animals demonstrate that the fibrinolytic system is indeed suppressed at the time of maximal activation of coagulation. Interestingly, in patients with acute promyelocytic leukemia, a severe hyperfibrinolytic state often occurs in addition to the coagulation activation. The release of several proinflammatory cytokines such as interleukin 6 and tumor necrosis factor α plays a central role in mediating the coagulation defects in DIC and symptoms associated with systemic inflammatory response syndrome (SIRS).

Clinical manifestations of DIC are related to the magnitude of the imbalance of hemostasis, to the underlying disease, or to both. The most common findings are bleeding ranging from oozing from venipuncture sites, petechiae, and ecchymoses to severe hemorrhage from the gastrointestinal tract, lung, or into the CNS. In chronic DIC, the bleeding symptoms are discrete and restricted to skin or mucosal surfaces. The hypercoagulability of DIC manifests as the occlusion of vessels in the microcirculation and resulting organ failure. Thrombosis of large vessels and cerebral embolism can also occur. Hemodynamic complications and shock are common among patients with acute DIC. The mortality ranges from 30 to >80% depending on the underlying disease, the severity of the DIC, and the age of the patient.

The diagnosis of clinically significant DIC is based on the presence of clinical and/or laboratory abnormalities of coagulation or thrombocytopenia. The laboratory diagnosis of DIC should prompt a search for the underlying disease if it is not already apparent. There is no single test that establishes the diagnosis of DIC. The laboratory investigation should include coagulation tests (aPTT, PT, thrombin time [TT]) and markers of fibrin degradation products (FDPs), in addition to platelet and red cell count and analysis of the blood smear. These tests should be repeated over a period of 6–8 h because an initially mild abnormality can change dramatically in patients with severe DIC.

Common findings include the prolongation of PT and/or aPTT; platelet counts μ100,000/μL, or a rapid decline in platelet numbers; the presence of schistocytes (fragmented red cells) in the blood smear; and elevated levels of FDP. The most sensitive test for DIC is the FDP level. DIC is an unlikely diagnosis in the presence of normal levels of FDP. The D-dimer test is more specific for detection of fibrin—but not fibrinogen—degradation products and indicates that the cross-linked fibrin has been digested by plasmin. Because fibrinogen has a prolonged half-life, plasma levels diminish acutely only in severe cases of DIC. High-grade DIC is also associated with levels of antithrombin III or plasminogen activity <60% of normal.

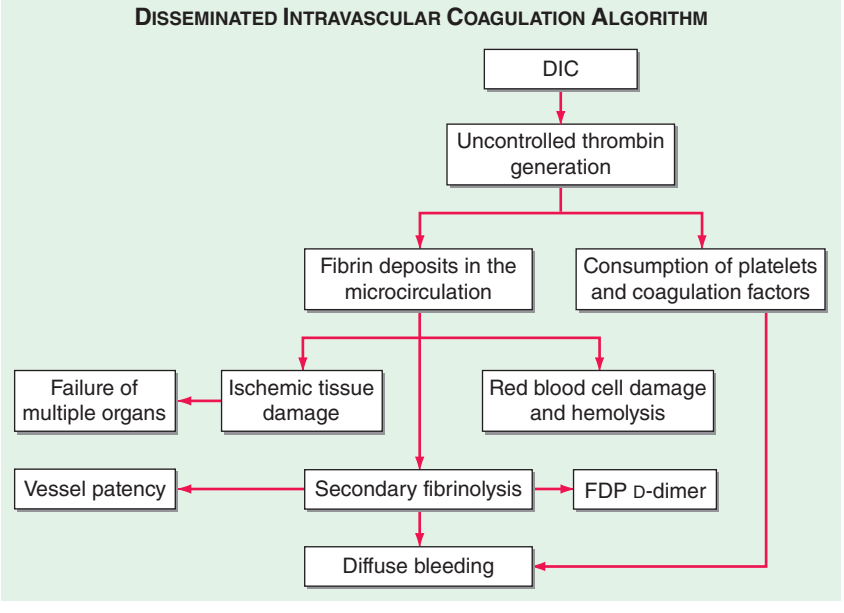

FIGURE 141-3 The pathophysiology of disseminated intravascular coagulation (DIC). Interactions between coagulation and fibrinolytic pathways result in bleeding and thrombosis in the microcirculation in patients with DIC. FDP, fibrin degradation product.