Clinical Features. The onset can be fulminant, as in endotoxic shock or amniotic fluid embolism, or insidious and chronic, as in cases of carcinomatosis or retention of a dead fetus. Overall, about 50% of the affected are obstetric patients having complications of pregnancy. In this setting the disorder tends to be reversible with delivery of the fetus. About 33% of the affected patients have carcinomatosis. The remaining cases are associated with the various entities previously listed.

It is almost impossible to detail all the potential clinical presentations, but a few common patterns are worthy of description. These include *microangiopathic hemolytic anemia*; dyspnea, cyanosis, and respiratory failure; convulsions and coma; oliguria and acute renal failure; and sudden or progressive circulatory failure and shock. In general, acute DIC, associated with obstetric complications or major trauma, for example, is dominated by a bleeding diathesis, whereas chronic DIC, such as occurs in cancer patients, tends to present with thrombotic complications. The diagnosis is based on clinical observation and laboratory studies, including measurement of fibrinogen levels, platelets, the PT and PTT, and fibrin degradation products.

The prognosis is highly variable and largely depends on the underlying disorder. The only definitive treatment is to remove or treat the inciting cause. The management requires meticulous maneuvering between the Scylla of thrombosis and the Charybdis of bleeding diathesis. Administration of anticoagulants or procoagulants has been advocated in specific settings, but not without controversy.

KEY CONCEPTS

Immune Thrombocytopenic Purpura

- Caused by autoantibodies against platelet antigens
- May be triggered by drugs, infections, or lymphomas, or may be idiopathic

Thrombotic Thrombocytopenic Purpura and Hemolytic Uremic Syndrome

- Both manifest with thrombocytopenia, microangiopathic hemolytic anemia, and renal failure; fever and CNS involvement are more typical of TTP.
- *TTP*: Caused by acquired or inherited deficiencies of ADAMTS 13, a plasma metalloprotease that cleaves very-high-molecular-weight multimers of von Willebrand factor (vWF). Deficiency of ADAMTS 13 results in abnormally large vWF multimers that activate platelets.
- *Hemolytic uremic syndrome*: caused by deficiencies of complement regulatory proteins or agents that damage endothelial cells, such as a Shiga-like toxin elaborated by *E. coli* strain O157:H7. The abnormalities initiate platelet activation, platelet aggregation, and microvascular thrombosis.

Von Willebrand Disease

- Autosomal dominant disorder caused by mutations in vWF, a large protein that promotes the adhesion of platelets to subendothelial collagen
- Typically causes a mild to moderate bleeding disorder resembling that associated with thrombocytopenia

Hemophilia

- *Hemophilia A*: X-linked disorder caused by mutations in factor VIII. Affected males typically present with severe bleeding into soft tissues and joints and have a PTT.
- *Hemophilia B*: X-linked disorder caused by mutations in coagulation factor IX. It is clinically identical to hemophilia A.

Disseminated Intravascular Coagulation

- Syndrome in which systemic activation of the coagulation leads to consumption of coagulation factors and platelets
- Can produce bleeding, vascular occlusion and tissue hypoxemia, or both
- Common triggers: sepsis, major trauma, certain cancers, obstetric complications

Complications of Transfusion

Blood products are often rightly called the gift of life, permitting people to survive traumatic injuries and procedures such as hematopoietic stem cell transplantation and complex surgical procedures that would otherwise prove fatal. Over 5 million red cell transfusions are given in US hospitals each year. Thanks to improved screening of donors, blood products (packed red blood cells, platelets, and fresh-frozen plasma) are safer than ever before.

Nevertheless, complications still occur. Most are minor and transient. The most common is referred to as a *febrile nonhemolytic reaction*, which takes the form of fever and chills, sometimes with mild dyspnea, within 6 hours of a transfusion of red cells or platelets. These reactions are thought to be caused by inflammatory mediators derived from donor leukocytes. The frequency of these reactions increases with the storage age of the product and is decreased by measures that limit donor leukocyte contamination. Symptoms respond to antipyretics and are short-lived.

Other transfusion reactions are uncommon or rare, but can have severe and sometimes fatal consequences, and therefore merit discussion.

Allergic Reactions

Severe, potentially fatal allergic reactions may occur when blood products containing certain antigens are given to previously sensitized recipients. These are most likely to occur in patients with IgA deficiency, which has a frequency of 1:300 to 1:500 people. In this instance, the reaction is triggered by IgG antibodies that recognize IgA in the infused blood product. Fortunately, most patients with IgA deficiency do not develop such antibodies, and these severe reactions are rare, occurring in 1 in 20,000 to 1 in 50,000 transfusions. *Urticarial allergic reactions* may be triggered by the presence an allergen in the donated blood product that is recognized by IgE antibodies in the recipient. These are considerably more common, occurring in 1% to 3% of transfusions, but are generally mild. In most instances symptoms respond to antihistamines and do not require discontinuation of the transfusion.

Hemolytic Reactions

***Acute hemolytic reactions* are usually caused by preformed IgM antibodies against donor red cells that fix**

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