Disseminated Intravascular Coagulation

**Feature**

**Synonyms**
DIC, consumption coagulopathy, consumptive thrombo-hemorrhagic disease, defibrination syndrome.

**Epidemiology**
DIC is one of the most common and clinically important acquired disorders of hemostasis. The true incidence of DIC is unknown because the disease is difficult to diagnosis. DIC occurs in acute and chronic forms of DIC.

**Pathogenesis**
DIC is widespread intravascular activation of the coagulation system ("runaway hemostasis") caused by a disruption in the intricate control mechanisms of hemostasis. DIC is not a specific disease, but the sequelae of many pathologic conditions with various effects on the hemostatic system (See Table). These conditions lead to release of proinflammatory cytokines, uncontrolled thrombin generation, widespread microvascular thrombosis, impairment of anticoagulant pathways, activation or impairment of the fibrinolytic system, and other effects. Tissue damage and the deposition of fibrin also result in the release and activation of plasminogen activators and the generation of plasmin in amounts that overwhelm its inhibitor, (alpha-2-antiplasmin). Plasmin degrades factors VIII, V, and I and produces fibrin/fibrinogen degradation products. These substances, as well as the products of incompletely polymerized fibrin, impair platelet function and normal fibrin polymerization. Microvascular thrombosis leads to tissue ischemia, necrosis, and organ dysfunction, and the release of tissue factor, which further accelerates the process. In acute DIC, the consumption of platelets and clotting factors occurs more rapidly than they can be replenished and bleeding results. The bleeding can be severe or even fatal. Chronic DIC ("compensated DIC," "nonovert DIC") occurs when time or intensity of the trigger mechanism is such that the the regulatory mechanisms of coagulation are able to control systemic activation of coagulation, and the liver and bone marrow are able replace the missing coagulation factors and platelets. The following table lists the pathogenic mechanism of DIC in different diseases.

<table>
<thead>
<tr>
<th>Disease</th>
<th>DIC Pathogenic Factors</th>
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<tbody>
<tr>
<td>Tissue damage, trauma</td>
<td>Release of thromboplastic substances with activation of extrinsic coagulation pathway. Increased proinflammatory cytokines with TF-mediated coagulation activation, suppression of anticoagulation, and PAI-1-mediated inhibition of fibrinolysis.</td>
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<tr>
<td>Shock</td>
<td>Decreased blood flow with loss of hemodilution. Ischemia and multiple organ failure.</td>
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<tr>
<td>Acute leukemia</td>
<td>Tumor cell-related factors with procoagulant and fibrinolytic properties, cytokine release by leukemia cells, effect of chemotherapy, infectious complications</td>
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**Clinical Presentation**

The clinical presentation and consequences of DIC depend on the etiology and the rapidity of the initiating event. Acute events lead to intravascular coagulation, with depletion of platelets and procoagulant factors, the production of fibrin degradation products, and bleeding. Slow or chronic activation of coagulation (compensated DIC, chronic DIC) leads to an excess of activated coagulation products, predisposing to thrombosis, vascular infarction, and venous thrombosis. DIC is more common in injured or seriously ill hospitalized than in outpatients. The usual signs include bleeding into deep tissues, as well as hemorrhage into wound sites, intravenous lines, and catheters. The intravascular fibrin strands produce microangiopathic hemolytic anemia. Fever, hypotension, acidosis, proteinuria, and hypoxia may also occur. Acute DIC may be fatal unless the condition is promptly diagnosed and appropriate treatment undertaken (DIC = “Death is Coming”).

**Laboratory Features**

*No single laboratory assay is pathognomonic of DIC.* Instead, the diagnosis must be made through consideration of both laboratory and clinical findings. Serial laboratory studies may be needed in early DIC. Thrombocytopenia is the usual laboratory finding leading to the consideration of DIC. Peripheral blood smear examination is essential, and shows a characteristic combination of thrombocytopenia, schistocytes, leukocytosis with a left shift, mild polychromatophilia, and large young platelets in fulminant cases. Unfortunately, schistocytes may be absent in chronic DIC. The bone marrow examination is contraindicated in DIC, but will show adequate megakaryocytes in spite of thrombocytopenia. Coagulation evaluation reveals a prolonged prothrombin time (PT) and activated thromboplastin time (aPTT), decreased fibrinogen and plasmin levels, and enhanced fibrinolysis, with elevated levels of fibrinogen degradation products (FDPs) and D-dimers.
Laboratory Features (Cont’d)

Of these laboratory tests, the D-dimer level is the most useful, since an elevated values indicate the formation and breakdown of fibrin thrombi. Unfortunately, elevated D-dimers levels are normally found after trauma, surgery, malignancy, and other conditions where DIC is common. A number of laboratory assays under evaluation focus on thrombin generation (i.e., prothrombin fragment 1+2), thrombin activation of the protein C and fibrinolytic pathways (i.e., activated protein C inhibitor and plasmin-antiplasmin complexes), and the end products of thrombin activity (i.e., fibrinopeptide A, soluble fibrin).

Treatment

The only definitive therapy for DIC is control of the initiating disease process. In the meantime, replacement of the deficient platelets and clotting factors is required, and the cautious use of heparin may reverse the cycle of consumption and clot formation. Otherwise, an uncontrollable, self-propagating clinical disaster of simultaneous bleeding and clotting can rapidly lead to the death of the patient. Until recently, FFP and/or cryoprecipitate were used to replace the missing clotting factors. However, clinical trials with antithrombin III, activated protein C, and tissue factor pathway inhibitor (TFPI) appear promising.

References


