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The Hospital Physician Hematology Board Review Manual is a study guide for fellows and practicing physicians preparing for board examinations in hematology. Each manual reviews a topic essential to the current practice of hematology.

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Disseminated Intravascular Coagulation

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INTRODUCTION

The process of coagulation is finely controlled at many levels to ensure the right amount of hemostasis at the right location. Broadly defined, disseminated intravascular coagulation (DIC) refers to any process that disrupts this fine tuning, leading to unregulated coagulation. Defined this way, DIC may be found in patients with a variety of diseases and can present with a spectrum of findings ranging from asymptomatic abnormal laboratory findings to florid bleeding or thrombosis. It is important to remember that DIC is always a consequence of an underlying pathological process and not a disease in and of itself. This manual reviews concepts common to all forms of DIC and discusses the more common disease states that lead to DIC.

PATHOGENESIS

At the most basic level, DIC is the clinical manifestation of inappropriate thrombin activation. Inappropriate thrombin activation can occur due to underlying conditions such as sepsis, obstetrical disasters, and trauma. The activation of thrombin leads to (1) conversion of fibrinogen to fibrin, (2) activation of platelets (and their consumption), (3) activation of factors V and VIII, (4) activation of protein C (and degradation of factors Va and VIIIa), (5) activation of endothelial cells, and (6) activation of fibrinolysis (Table 1).

Conversion of fibrinogen to fibrin leads to formation of fibrin monomers and excessive thrombus formation. These thrombi are rapidly dissolved by excessive fibrinolysis in most patients, but in certain clinical situations, especially cancer, excessive thrombosis will occur. In patients with cancer, this is most often a deep venous thrombosis, and rarely patients may have severe DIC with multiple arterial and venous thromboses, especially patients with pancreatic cancer. Nonbacterial thrombotic endocarditis can also be seen in these patients.

Because thrombin is the most potent physiologic activator of platelets, there is increased activation of platelets in DIC. These activated platelets are consumed, resulting in thrombocytopenia. Platelet dysfunction is also present. Platelets that have been activated and have released their contents but still circulate are known as "exhausted" platelets; these patients can no longer function to support coagulation. The fibrin degradation products (FDP) in DIC can also bind to GP IIb/IIIa and further inhibit platelet aggregation.

Activation of factors V, VIII, XI, and XIII can promote thrombosis, but they are then rapidly cleared by antithrombin (XI) or activated protein C (V and VIII) or by binding to the fibrin clot (XIII). This can lead to depletion of all the prothrombotic clotting factors and antithrombin, resulting in both thrombosis and bleeding.

Activation of protein C further promotes degradation of factors Va and VIIIa, enhances fibrinolysis, and decreases protein C levels. Activation of endothelial cells, especially in the skin, may lead to thrombosis. Purpura fulminans also may develop in certain patients, especially those with meningococcemia. Endothelial damage will downregulate thrombomodulin, preventing activation of protein C and leading to further reductions in levels of activated protein C.

Finally, activation of fibrinolysis leads to breakdown of fibrin monomers, formation of fibrin thrombi, and increased levels of circulating fibrinogen. In most patients with DIC, the fibrinolytic response is brisk, which explains why most patients with DIC present with bleeding and prolonged clotting times.

PATTERNS OF DIC

The clinical manifestations of DIC in a given patient depend on the balance of thrombin activation and secondary fibrinolysis as well as the patient’s ability to compensate for the DIC. Patients with DIC present in 1 of 4 patterns: they can be asymptomatic, presenting with laboratory evidence of DIC but no bleeding or thrombosis, or present with overt bleeding, thrombosis, or purpura fulminans. Asymptomatic presentation is often seen in patients with sepsis or cancer. However, these patients can rapidly become symptomatic with progression.