Inflammation is associated with thrombotic predisposition in patients. The mechanisms by which inflammation contributes to the thrombosis involve both humoral and cellular changes. Inflammation impacts all phases of blood coagulation: initiation, propagation and the inhibition. Inflammatory mediators like endotoxin and tumor necrosis factor alpha induce expression of tissue factor on blood cells, particularly monocytes. Tissue factor then triggers the initiation of coagulation. Normally, negatively charged membrane surfaces are limiting so that even if some activated coagulation factors are generated, they fail to propagate coagulation. C reactive protein, an acute phase reactant, levels increase in response to inflammation. The C reactive protein can then induce tissue factor formation. Complement membrane attack complex provides a potent stimulus for cells to express negatively charged phospholipid on their outer membrane leaflet. Alternatively, exposure to collagen in combination with thrombin provides a potent stimulus to platelets eliciting the formation of microparticles and the subsequent exposure of negatively charged phospholipid membrane surfaces that can propagate coagulation. Even when these two events both occur to augment coagulation, potent natural anticoagulant mechanisms limit the thrombotic response. Inflammatory mediators, however, can depress these potent natural anticoagulant mechanisms. Of the natural anticoagulants, the protein C pathway is one of the systems down regulated by inflammation. Thrombomodulin and the endothelial cell protein C receptor are both required for optimal protein C activation in response to thrombin generation. In severe inflammatory situations, both proteins are down regulated resulting in a decreased anticoagulant response. Furthermore, free protein S levels often decrease, further impairing the pathway. In immune mediated inflammatory disease, the pathway may also be down regulated. Some anti-phospholipid antibodies severely impair the protein C pathway. Clinically relevant thrombosis is minimized naturally either by inhibiting the blood clotting or by rapid lysis of the blood clot or both. In addition to shifting the hemostatic balance in favor of clot formation, inflammation elevates plasminogen activator inhibitor levels resulting in decreased fibrinolytic activity. Procoagulant impacts of inflammation are also expressed at the cellular level. Interleukin 6 can increase platelet numbers and their responsiveness to agonists like thrombin. All of these events tend to shift the hemostatic balance in favor of clot formation.