Looking toward the future: Treatment of bleeding episodes in the pediatric population

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There have been significant advances in the field of coagulation in recent years leading to the discovery of previously poorly understood mechanisms of throbmogenesis. In the past, the classic coagulation cascade was felt to represent the steps involved in fibrin formation and was widely taught and presented in textbooks, manuscripts and monographs. While understanding the steps of the classic cascade are useful in assessing the differential diagnosis of a prolonged prothrombin or activated partial thromboplastin time, it is now clear that this cascade does not represent in vivo fibrin formation. The remodeled coagulation system depends on the interaction of factor VIIa with exposed tissue factor at the site of bleeding which then leads to an initial formation of a small amount of thrombin. This small amount of thrombin activates factors V and VIII as well as platelets and the activated factors V and VIII then catalyze the conversion of a large amount of prothrombin to thrombin leading to generation of large amounts of thrombin on the surface of the activated platelet at the site of bleeding. This new theory of coagulation explains the fact that deficiencies of factors VIII and IX lead to severe bleeding disorders something the classic cascade could not explain.

The understanding of the new mechanism of coagulation has lead to the a better understanding of the pathophysiology of bleeding and subsequently to improved methods to control hemostasis. There are 2 new hemostatic agents (one commercially available and one in clinical trials) with significantly improved properties over fresh frozen plasma, cryoprecipitate and other agents which have shown promise as universal hemostatic agents. The first rFVIIa, currently licensed for the management of hemophilia patients with inhibitors to factor VIII or IX, which has been extensively utilized in a variety of clinical settings to enhance hemostasis. I will discuss the proposed mehcanism of action of this agent as well as the various clinical settings it has been used in to establish hemostasis. The second agent, factor XIII concentrate is currently in clinical trials for factor XIII deficiency and in cardiopulmonary bypass. It has the potential to be useful in a variety of clinical settings as well, and will be discussed as another novel hemostatic agent.