Care of children with hemophilia should always involve specialized physicians working within a multidisciplinary treatment team, especially when severe bleeding or inhibitors develop. In addition, these children should be periodically evaluated at hemophilia centers. Pregnant carriers of the hemophilia gene should undergo prenatal counseling with a hemophilia specialist regarding childbirth.

Rare Coagulation Disorders

Clinically significant congenital deficiencies of fibrinogen, prothrombin, Factor V, combined Factor V/VIII, Factor VII,Factor X, Factor XI, Factor XIII, combined vitamin-K-dependent factors (II, VII, IX, and X), and the contact factors are rare, and usually inherited as autosomal recessive traits. Clinically these may present with mucocutaneous bleeding, increased bleeding with surgery or childbirth, or, occasionally, life- or limb-threatening bleeding, the last more commonly associated with deficiencies of fibrinogen, Factor X, and Factor XIII.[92] The measurement of plasma factor activity may predict the severity and frequency of clinical manifestations, but the relationship between factor levels and bleeding tendency is sometimes poor, particularly for Factor VII and Factor XI deficiencies.[93] (See Table 23 for details.)

Of note, Factor XII, prekallikrein, and high-molecular-weight kininogen may be protective against thrombus formation but have no effect on hemostasis, and deficiencies are not associated with a bleeding diathesis.[99]

Like the more common bleeding disorders, treatment strategies include factor replacement and antifibrinolytics. EACA and tranexamic acid can be used orally, topically, and intravenously.[94] Generally, neonates and children with single-factor deficiencies should be treated with either recombinant or plasma-derived concentrates for the specific factor whenever available, which allows the administration of adequate and precise doses in relatively small volumes.[92] (See Table 23.) In addition, unlike plasma or Cryoprecipitated AHF, these products have been treated to minimize the risk of viral disease transmission.

Table 23. Clinical Features and Management of Bleeding of the Rare Coagulation Disorders*

Deficient Factor	Main Bleeding Symptoms†	Therapeutic Target Trough Levels for Surgery[94]	Plasma Half-Life	On-Demand Treatment†	Treatment for Major Surgery
Fibrinogen	Umbilical cord, joint, mucosal; bruising; severe, from birth trauma or surgery	>100 mg/dL	2-4 days	Fibrinogen concentrate (50-100 mg/kg) Cryoprecipitate (15-20 mL/kg) Plasma‡ (15-30 mL/kg)	Every 24-48 hours for 4-6 days
Prothrombin	Umbilical cord, joint, mild mucosal, surgical	>20 IU/dL	3-4 days	PCC (20-40 U/kg) Plasma‡ (15-25 mL/kg)	Every 48 hours
FV	Mucosal, surgical; moderately severe in homozygotes	>15-20 IU/dL	36 hours	Plasma (15-25 mL/kg) Platelets	Every 12 hours if needed
FVII	Mucosal, joint (may be severe), muscle, surgical; levels may correlate poorly with symptoms	>20 IU/dL	4-6 hours	rFVIIa (15-30 mcg/kg) 4-factor PCC (30-40 U/kg) Plasma‡ (10-20 mL/kg)	Every 4-6 hours for 24 hours, then every 8-12 hours for rFVIIa

FX	Epistaxis/mucosal, umbilical cord, joint, muscle, surgical; may be severe	>20-30 IU/dL	40-60 hours	PCC (20-30 U FX/kg) Plasma‡ (10-20 mL/kg) FX concentrate (25 U/kg)	Every 24 hours
FXI	Posttraumatic; variable with different surgeries, epistaxis	15-20 IU/dL	50 hours	Antifibrinolytic in patients with previous surgical bleeding Plasma‡ (15-20 mL/kg) FXI concentrate (15-20 mL/kg, not available in US)	
FXIII	Umbilical cord, intracranial, joint, recurrent miscarriages, surgical, delayed bleeding	>20 IU/dL	9-12 days	Plasma-derived FXIII concentrate (20-40 U/kg) Recombinant FXIII-A (35 U/kg) Cryoprecipitate (1 unit/10 kg body weight) Plasma‡ (10-15 mL/kg)[95,96]	Every 24 hours

(continued)