### Factor XIII Deficiency

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#### Feature

<table>
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<th><strong>Synonyms</strong></th>
<th>Fibrin stabilizing factor deficiency.</th>
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<td><strong>Epidemiology</strong></td>
<td>Very rare disorder, true incidence unknown since heterozygous carriers and patients with mild deficiency usually go undetected.</td>
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<td><strong>Pathogenesis</strong></td>
<td>Factor XIII consists of two nonidentical-polypeptide subunits, the &quot;a&quot; chain and the &quot;b&quot; chain, that form a tetrameric molecule comprised of two a chains and two b chains (320,000 daltons). Activation of the factor XIII molecule by thrombin and calcium results in exposure of an active cysteine residue on the a chains, followed by dissociation of the b chain dimer. The activated form of factor XIII catalyzes the formation of covalent bonds between the gamma chains and alpha chains of fibrin, resulting in greatly increased mechanical stability and enhanced resistance of the fibrin clot to dissolution, fibrinolytic digestion by plasmin and non-specific proteolysis. Some of the inhibitors of fibrinolysis, such as alpha-2-plasmin inhibitor, are also stabilized by factor XIII. Only homozygous-recessive patients with severe deficiencies have clinical symptomatology, since plasma factor XIII levels of 1% to 2% or more are adequate for fibrin stabilization. Homozygous-recessive patients lack the a chains and have normal, reduced, or absent b chain antigenicity normally present in plasma. A specific factor XIII mutation, Val[34]Leu, is present in many patients with symptomatic factor XIII deficiency. Patients with dysfunctional factor XIII molecules have not been described.</td>
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<td><strong>Pattern of Inheritance</strong></td>
<td>Usually inherited as an autosomal recessive trait, but rare families have been described in which only males are affected.</td>
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<td><strong>Clinical Presentation</strong></td>
<td>Patients with homozygous recessive factor XIII deficiency are detected during the neonatal period due to umbilical cord bleeding. These patients also have an increased prevalence of primary intracranial hemorrhage, which is frequently fatal. Ecchymoses, hematomas, hemarthroses, and prolonged bleeding after superficial wounds, dental extractions or surgery. Poor wound healing with excessive scar formation is seen in some patients but is not a consistent feature of the disease. In contrast, epistaxis, gingival bleeding, hematuria, and menorrhagia are not commonly seen. Spontaneous bleeding is not found in patients with a factor XIII level &gt;3%. Clinical symptomatology is absent from individuals with heterozygous FXIII deficiency. Acquired decreases in factor XIII activity is seen in a few diseases, including the acute stages of Henoch Schonlein purpura (HSP) and the active stages of ulcerative colitis and Crohn’s disease. Inhibitors against factor XIII have rarely been described.</td>
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**Laboratory Features**

The platelet count, bleeding time, prothrombin time, aPTT, thrombin time, and whole blood clotting time are within normal limits. The diagnosis is usually based on the clot stability test, although specific immunoassays for factor XIII exist.

The clot stability test is based on the principle that the unstabilized clots in factor XIII patients are rapidly dissolved in 5 M urea or 1% monochloroacetic acid, while factor XIII-stabilized clots will be resistant to dissolution under these circumstances. Since a factor XIII level of 1% will produce clot stabilization and a normal clot stability test, heterozygotes and patients with mild deficiency must be detected by quantitative (immunologic) assays. Dysfibrinogenemia, lead poisoning, mercury poisoning, and hyperfibrinolysis can prevent clot stabilization and must be excluded in patients with an abnormal clot stabilization assay.

**Treatment**

Factor XIII deficiency is treated with cryoprecipitate or fresh frozen plasma (FFP). Due to the low concentrations of factor XIII required for hemostasis, and the long half-life of factor XIII, prophylactic infusions are required at long (4-5 week) intervals.

**References**