## Factor IX Deficiency

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**April, 2005**

### Feature | Disease Facts
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**Synonyms** | Hemophilia B, Christmas disease, plasma thromboplastin component (PTA) deficiency.

**Epidemiology** | The incidence of factor IX deficiency is 1 in 30,000 male births. Factor IX deficiency was independently described in 1952 by three different groups of investigators and named Christmas disease after the first patient of one Dr. Rosemary Bigg’s group.

**Etiology and Pathogenesis** | Factor IX is a single-chain, vitamin K-dependent glycoprotein serine protease with a molecular weight of approximately 55,400 and a plasma concentration of 3 – 5 µg/mL. Factor IX is encoded by a 34-kb gene located near the terminal end of the long arm of the X chromosome. Factor IX is activated by factor XIa, factor VIIa, or by Russell’s viper venom. Activated factor IX (IXa) forms a complex with activated factor VIII, calcium and phospholipid which activates factor X. Most inherited abnormalities of factor IX are caused by a true deficiency, but a few patients with a dysfunctional form of the molecule have been identified. Factor IX disease is extremely heterogenous, with nearly 700 point mutations, additions, deletions, and other molecular abnormalities identified in different patients.

**Pattern of Inheritance** | X-linked recessive.

**Clinical Presentation** | The clinical severity of factor IX deficiency is determined by the plasma level of factor IX (severe: <1%, moderate: 1%-5%, mild: 5%-25%). The clinical manifestations are identical to those of hemophilia A (factor VIII deficiency). The most serious complication in hemophilia B is the development of antibodies (inhibitors) to factor IX (10% of patients with hemophilia B).

**Laboratory Features** | Patients with factor IX deficiency typically have a prolonged aPTT that is corrected by an equal volume of normal plasma (1:1 mixing study). However, patients with mild factor IX deficiency may have normal or nearly normal aPTT results, depending on the sensitivity of the laboratory performing the analysis. As a consequence, assays of factor IX coagulant activity (“factor IX levels”) should be performed if the disease is clinically suspected, even with a normal aPTT. Factor IX coagulant activity is determined by the conventional one-stage aPTT assay, using factor IX deficient plasma as the substrate. If necessary, quantitative levels of factor IX can be measured by immunologic techniques, and activated factor IX can be determined with chromogenic substrates.

**Treatment** | Replacement therapy to raise the plasma factor IX level to the therapeutic range is the basis of factor IX therapy. Preferred factor IX replacements at the present time include recombinant factor IX and purified, virus-free factor IX concentrate prepared from pooled human plasma.
**Treatment (Cont’d)**

**Prothrombin-complex concentrates** (PCC) can also be used, but are associated with an increased risk of thrombotic complications. **Fresh frozen plasma** (FFP) is another alternative, but it is difficult to achieve therapeutic factor IX levels without volume overload. Gene therapy is under development and may become the treatment of choice in the future.

The development of inhibitors (antibodies) to factor IX is an uncommon, but serious complication in factor IX therapy. Inhibitors develop in 3-10% of treated patients, usually in association with a severe factor IX deficiency. Life-threatening anaphylactoid reactions have been reported in patients with factor IX inhibitors. Immune tolerance induction (ITI) can be used to desensitize patients with anaphylactoid reactions, but there is a risk of developing steroid-resistant nephritic syndrome..

**References**


