

Immunological heterogeneity of haemophilia B: a multicentre study of 98 kindreds.

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An electroimmunoassay with a precipitating rabbit anti-human factor IX antiserum and an inhibitor neutralization assay with a non-precipitating homologous antibody were used to measure factor IX antigen (IX:Ag) in 117 patients from 98 kindreds with haemophilia B; and to investigate in a mixed population the incidence of different immunological types of the disease. Although the two assays showed an excellent correlation, the electroimmunoassay was selected for its simplicity as a criterion for classification. 52 kindreds, referred to as haemophilia B-, were characterized by severe deficiency of factor IX coagulant activity (less than 0.01--0.03 u/ml) and unmeasurable IX:Ag (less than 0.12 u/ml): this genetic variant of the disease appears to be related to a complete or marked suppression of factor IX synthesis. In 16 kindreds, a severe or moderately severe IX:C deficiency was associated with normal or increased levels of IX:Ag (haemophilia B+): among them, a subgroup of five kindreds could be identified by the additional abnormality of a prolonged Thrombotest clotting time (haemophilia BM). These patients are likely to be the expression of normal or increased synthesis of a factor IX molecule markedly defective in the site(s) responsible for coagulant activity. Reduced levels of IX:Ag (0.12--0.65 u/ml, characterized the remaining 30 kindreds, presenting with IX:C levels ranging from less than 0.01 to 0.21 mu/ml. In 28 there was a significant excess of IX:Ag over IX:C, suggesting a reduced capacity to synthesize the factor IX molecule accompanied by a variable defect in the coagulant site; the remaining two kindreds, which showed a concomitant reduction of IX:C and IX:Ag, are likely to be examples of a true reduction of factor IX synthesis.