The Prevalence of Plasma Thromboplastin Antecedent (PTA, Factor XI) Deficiency

By W. Angus Muir and Oscar D. Ratnoff

PLASMA THROMBOPLASTIN antecedent (PTA, Factor XI) deficiency is an inherited disorder of blood coagulation characterized by a defect of the intrinsic pathway of thrombin formation and a mild to moderate bleeding tendency. Since the original description by Rosenthal, Dreskin, and Rosenthal, it has been reported in this country and in Europe to occur with especial frequency in Jewish individuals.

The mode of inheritance of PTA deficiency has been disputed, but the bulk of data suggest that it is transmitted as an autosomal recessive trait. Since the prevalence of PTA deficiency and of the carrier state is unknown, we have reviewed our experience with PTA deficiency in Cuyahoga County, Ohio, of which Cleveland is the county seat.

The patients participating in this study were referred to us either because of a mild to moderate bleeding diathesis, revealed by dental extractions or by minor surgical procedures, or because a prolonged partial thromboplastin time was found during routine studies. None of the patients bled spontaneously, and the extent of bleeding was limited to local oozing for 3–14 days after surgical procedures. All patients had a prolonged partial thromboplastin time. The concentration of PTA in different patients ranged from 0.01 to 0.08 U/ml of plasma; pooled normal plasma contains 1.0 U/ml, while the PTA content of individual normal plasmas varies from 0.55 to 1.85 U/ml as tested in this laboratory. All available close relatives of PTA-deficient patients were tested for PTA activity.

We have identified seven patients with PTA deficiency in Cuyahoga County, all of Jewish origin; two of the patients were sibs. The pattern of inheritance was not always established in these cases due to a paucity of family data. In one parent and eight offspring of PTA-deficient individuals, the concentration of PTA varied from 0.33 to 0.96 U/ml, averaging 0.49 U/ml. Similar data were obtained in a carefully studied family from a nearby county. These data are consistent with the assumption that in most instances PTA deficiency is inherited as an autosomal recessive trait.

A recent estimate indicates that in 1973, 83,000 individuals in Cuyahoga County were identified as Jewish. Accepting this figure, the minimal prevalence of homozygous PTA deficiency is approximately 1/12,000. Using the principle

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of the Hardy-Weinberg law, the minimal prevalence of the carrier state for PTA deficiency in the Jewish population of Cuyahoga County is $1/56$. Since PTA deficiency produces few symptoms, it is probable that some have been overlooked, and that therefore both the prevalence of homozygous PTA deficiency and of the heterozygous (carrier) state is higher than we have estimated. The high fitness and the apparent high frequency of the carrier state for PTA deficiency suggests that the mutation responsible might have occurred in remote times. After the Roman conquest of Judea in the first century A.D., the Jewish population was widely dispersed. All of our patients were of European origin. Ramot, however, has described a Jewish patient with PTA deficiency born in Iraq and recently observed at least one other patient who may also have been of non-European stock. If these observations are correct, the original mutation may well have occurred in the distant past. The high frequency of the carrier state for PTA deficiency approaches that observed in Tay-Sachs disease and identifies a second frequent, albeit much less severe, hereditary abnormality in this population.

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