SYMPOSIA SESSION

III Molecular Problems of Factor IX

MUTANT FORMS OF FACTOR IX. H. R. Roberts, K. S. Chung and J. C. Goldsmith. University of North Carolina School of Medicine, Chapel Hill, North Carolina, U.S.A.

Evidence for the heterogeneity of hemophilia B is based on the observation that differing abnormal Factor IX molecules can be isolated and characterized from certain patients with hemophilia B. The abnormal molecules, so far studied, are present in virtually normal amounts when measured by immunological techniques, but have reduced clotting activity. Other hemophilia B patients have reduced concentrations of antigenically detectable Factor IX as well as reduced clotting activity. Still other hemophilia B patients have no detectable Factor IX, either by immunological techniques or by functional assays.

The purpose of this report is to describe another kindred with two affected members who have an abnormal Factor IX molecule. The affected members have a bleeding disorder typical of moderate hemophilia B. However they have a normal prothrombin time (PT) and an only slightly prolonged partial thromboplastin time (PTT). The PTT becomes markedly prolonged when the lipid employed in the assay is diluted. Factor IX can be detected in the affected patients by immunological techniques and has recently been isolated by purification procedures involving,as a final step, heparin agarose affinity chromatography. This abnormal Factor IX, tentatively named Factor $IX_{Alabama}$, differs from Factor IX_{BM} (prolonged PT and PTT) and Factor $IX_{Chapel\ Hill}$ (prolonged PTT and normal PT). Thus, the heterogeneous nature of Factor IX is being elucidated and clarified.

FACTOR IX LEVEL IN VARIOUS CONDITIONS. J.J. Veltkamp. University of Leiden Medical School, Hemostasis and Thrombosis Research Unit, Leiden, The Netherlands.

In newborns the factor IX level is only 20-60% of that observed in adults. This implies that factor IX levels have to increase with age, as was demonstrated already by Simpson and Biggs (1962). A rapid rise might occur in the first year of life, as is the case for albumen. During life, then, a slow rise continues, as was also demonstrated for factors V and VII (Brozovic 1976, 1974). It is of special interest that for factors VII and IX, both vitamin K dependant clotting factors, not only age but also hormones influence the activity level. Both the oestrogen containing contraceptive pill and pregnancy cause a substantial rise in factor IX level, both activity and CRM. 7 Years ago we started to measure factor IX levels every 3 months in 10 children, now at the age of 19, to see whether an abrupt rise would occur during puberty; this was not so. This information was considered relevant for the explanation of the appearance of factor IX activity and CRM in patients with hemophilia B Leyden during puberty. After a rise from <1% to 20% factor IX in the age period from 15 to 20 factor IX continues to rise at a slower rate and may reach 50% in old age. Clinical symptoms disappear. There is no good explanation for this phenomenon that occurs in patients from two probably related kindreds with hemophilia B in The Netherlands.