**CONGENITALLY ABNORMAL FIBRINOGENS**

**FIBRINOGENS NEW YORK I AND LA HAVE BEEN PURIFIED FROM BLOOD PLASMAS OF SISTERS AND A BROTHER IN A WHITE FAMILY WITH THROMBOTIC TENDENCY.** Both are heterozygous and carry both thrombophilic fibrinogens with two normal a-chains and thrombin-nontocleltable fibrinogen with two abnormal a-chains. The abnormal a-chains result from deletions of amino acid residues 9-72, which are encoded exactly by exon 111 of the gene. Studies of the genetic disorder for this deletion, genomic DNAs were isolated respectively from leukocytes of NY-Ia, NY-Ib (a nonaffected brother), and two normal individuals outside the NY-I family, and analysed in Southern blotting experiments with a human genomic DNA probe containing exon 111. Digestion of various DNAs were performed with two different restriction enzymes, and these digestions were analysed respectively by agarose electrophoresis.

Deletion with Hind III reveals 3 cleavage sites (one site in intron A near exon 111) with formation of two fragments of equal size (2 bands: 3.1 kb and 3.1 kb) in normal, NY-Ia and NY-Ib, but an extra fragment (one used = 6.0 kb) in NY-Ia. Deletion with Pst I reveals 3 cleavage sites (one site in exon 111) with formation of two fragments (2 bands: 7.5 kb and 2.9 kb) in normal, NY-Ia and NY-Ib, but an extra fragment (one used = 5.7 kb) in NY-Ia. These results show that one Hind III and one Pst I cleavage site which are present in the normal allele are absent in the abnormal allele of NY-Ia. Thus, these studies indicate that the genetic defect in the abnormal allele is near the junction of intron A and exon 111. It is possible that this genomic disorder is associated with the patient (NY-Ia) with a thrombotic tendency, and further suggest that the genetic defect in the abnormal allele is near the junction of intron A and exon 111. In conclusion, the possible usage for this genomic disorder is due to that an inverse double crossover have taken place in a region covering this junction, resulting in a normal mRNA and a novel protein product. This novel protein product is otherwise deleterious to fibrinogen, and may cause a thrombotic tendency.

**ABNORMAL FIBRINOGEN (FIBRINOGEN MAPLES) CHARACTERIZED BY DEFECTIVE INTRA- AND INTER-PMER FIBRINOGEN DEGRADATION WITH ARTERIAL THROMBOSIS.** G. Di Minno, A.M. Ceronbe, F. Cirillo, M. Colucci, N. Senegaro, D. Sisto, P.L. Mattoli, M. Mancini and M. Vasciavo (Fondazione Ingoglio California University at Catanzaro and Department of Internal Medicine and Metabolic Disease, II Medical School, Naples University, and Department of Clinical Pathology, Bari University, Italy).

Prolonged thrombin time (partially corrected by calcium chloride) and normal platelet count time were found in the plasma of two siblings with arterial thrombosis. Their purified fibrinogens showed similar abnormalities as well as impaired fibrinogenase release in response to thrombin, delayed polymerization of pre-formed fibrin monomers and normal sialic content. Binding of radiolabelled thrombin by patient's fibrin was 30% of normal. Supernatants from patients' fibrin clots contained abnormal amounts of fibrinogen (not adsorbed by fibrinogen) and caused abnormal enhancement of platelet aggregation and ATP secretion from platelets exposed to sub-threshold concentrations of ADP or epinephrine. Hirudin suppressed the enhancing effect of the supernatant and substitution of fibrinogen for d-thrombin led to normalization of platelet response. Studies on fibrinolysis showed that the abnormal fibrinogen from these patients as well as its naturally occurring derivative fibrin are highly resistant to lysis by plasmin. Thus our data support the concept that, in addition to the enhanced activation of platelets by radiolabelled thrombin, thrombosis in these patients is the result of an impaired sensitivity of fibrinogen the lytic effect of plasmin.