

FIBRINOGEN, FIBRINOGEN HETEROGENEITY AND FIBRINOLYTIC ACTIVITY IN DIABETES MELLITUS.

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Fibrinogen (F) concentration, fibrinogen heterogeneity on 3.5% polyacrylamide gels, fibrinolytic activity (FA) measured by euglobulin fraction on fibrin plates and fibrin degradation products (FDP) were measured in 66 patients with well documented diabetes mellitus (DM) and in 50 healthy subjects of comparable age. A high molecular weight and 2 lower molecular weight (LMW and LMW¹) fibrinogen fractions were identified. The mean values and statistical evaluation of their differences were as follows:

	CONTROLS		DM
F	370	p<0.01	470 mg%
LMW	96	<0.01	143 mg%
LMW ¹	6	<0.001	39 mg%
FDP	5	<0.01	32 µg/ml
FA	56	<0.001	26 mm

The clinical duration of DM, degree of control or type of medication did not appear to influence these findings. However, within the patient group, those with clinical evidence of microvascular disease had significantly (p<0.02) higher LMW¹ fibrinogen and lower FDP (p<0.01) than the remainder. These findings suggest that DM is associated with fibrin deposition, and accelerated F degradation to LMW and LMW¹ fractions and that these processes may be associated with the development of vascular lesions.

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CONGENITAL DYSFIBRINOGENEMIA. (FIBRINOGEN OSLO II). H.C. Godal, F. Brosstad and P. Kierulf. Haematological Research Laboratory, Department IX, Ullevål Hospital University Clinic, Oslo, Norway.

An autosomally inherited, qualitative fibrinogen defect, associated with prolonged thrombin clotting time, low plasma fibrinogen when assayed by a fibrin polymerization test and large amounts of fibrinogen antigen determinants in the supernatant after clotting, is presented. The plasma fibrinogen level was normal when assayed by an immunological technique or by quantitation of insoluble fibrin under conditions in which fibrin polymerization is enhanced. As judged from N-terminal amino acid analyses, fibrinopeptides were split off at normal speed, and the subunit chains of the fibrinogen appeared normal when examined on polyacrylamide gels. The abnormality was not associated with bleeding tendency, and other routine coagulation tests gave normal results. The findings are in accordance with the concept of defective fibrin polymerization.

INTERACTIONS OF HUMAN FIBRINOGEN IN SOLUTION. E. Serrallach, W. Känzig. Dept. of Physics, ETH-Zürich. V. Hofmann, P.W. Straub. Dept. of Medicine, University of Berne. M. Zulauf. Biozentrum, Basle, Switzerland.

The intriguing diversity of published translational diffusion constants for the fibrinogen molecule can hardly be explained, unless interactions between the molecules are postulated. In the present study we have investigated the possible effect of molecular association and electrostatic intermolecular interactions on the Brownian motion. The translational diffusion coefficient D_T , the rotational diffusion coefficient around the minor axis D_R and the sedimentation coefficient have been measured. The methods used were dynamic light scattering and analytical ultracentrifugation. The samples were solutions of purified human fibrinogen. The correlation-function corresponding to D_T deviates from a single exponential. The initial slope is found to depend on concentration, being $D_T = (1.7 \pm 0.3) \cdot 10^{-7} \text{ cm}^2/\text{s}$ at 10mg/ml, pH 7.4 and 0.15 molar Tris-NaCl, and increases at fibrinogen concentrations below 2mg/ml. These results are compatible with a polydisperse solution, in which single molecules are in equilibrium with pair and higher aggregates. The nature of the aggregates is end-to-end as indicated from the difference between the two rotational diffusion constants $D_R = 40000 \pm 20\%$ and $D_R = 10000 \pm 30\%$ s⁻¹. On the basis of the Hall-Slayter model and assumption of end-to-end association we calculated the ratio of the sedimentation coefficient of single, pair and triplet associates, being 1:1.14:1.20. Therefore, it is difficult to separate them in a sedimentation run. For ionic strength below 0.05 molar and low fibrinogen concentration (0.1mg/ml) a fast decay appears in the correlation, indicating that the Brownian motion is strongly influenced by electrostatic interactions.