of the two techniques whereas the remaining eight patients had CRM varying from low to normal values. The coefficient of correlation was 0.82 between the determinations of CRM by the two techniques.

One of the patients with severe haemophilia and normal amounts of plasma CRM showed a prolonged prothrombin time using ox brain thromboplastin (haemophilia B_M). As a group, the other patients had a significantly reduced prothrombin time when compared to 20 healthy males.

Our results confirm that haemophilia B is a heterogeneous disorder and show that the EIA may be used to detect genetic variants of this disease.

M. Matsuoka, M. Ito, N. Sakuragawa and K. Takahashi (Niigata University School of Medicine, 951 Niigata, Japan): **Immunological Method for the Detection of the Carrier of Haemophilia B.** **(23)**

Both the immunoassay and bioassay were performed on factor IX activity of haemophilia B patient. Their values were compared with each other.

The immunoassay by neutralization was performed as follows: antibody to factor IX was obtained by immunization of purified factor IX to rabbit which was isolated by the technique of DEAE-Sephadex column chromatography using eluate from $BaSO_4$ which absorbed factor IX of normal human plasma.

In approximately 90% of the cases of definite carriers of haemophilia B, the activity of factor IX by bioassay was observed to be lower than that of factor VIII of haemophilia A carrier. The factor IX activity was observed to be at the same level as factor IX antigen by immunoassay in almost all of the cases, but in the cases of the mother of haemophilia B, and the North Carolina type of haemophilia B the factor IX antigen was much greater than that of activity by bioassay. The same results were obtained by the above mentioned methods using inhibitor substance arising from severe haemophilia B patient.

It was suggested that the immunoassay method is useful in detecting the carrier of haemophilia B and North Carolina type of haemophilia B.

P. A. Castaldi and K. M. McGrath (Austin Hospital and University of Melbourne, Melbourne, 3084, Australia): **Cyclical Variation in Factors VII and VIII Associated with Oral Contraception.** **(24)**

Sequential studies of the levels of coagulation factors II, VII, VIII (activity and antigen), IX, X and fibrinogen, were carried out in three females using oral contraceptive agents, and two normal controls. A striking increase in the levels of factor VII activity was seen in the second half of the menstrual cycle in all test subjects. In two test subjects, a marked cyclic increase in factor VIII activity occurred and this did not have any fixed relationship to VIII antigen levels.

The increase in factor VII activity was associated with shortening of the thrombotest in plasma tested after storage at –20 C. Activation of factor VII can be induced in vitro in 60% of oral contraceptive plasmas by incubation at 4 C for 16 hours. This cold promoted activity (CPA) also varies throughout a menstrual cycle, is independent of the prothrombin complex, being present in Al_2OH_3 adsorbed plasma, and is contained in the supernatant of the euglobulin fraction in CPA positive plasmas. It can induce activation of factor VII in normal plasma, but not in contact factor deficient plasma. The nature of this cold sensitive activity and its relationship to the cyclical increase seen in factor VII activity and to oestrogen induced clotting in vivo, remains to be determined.

K. Miloszewski and M. S. Losowsky (St. James's Hospital, Leeds LS9 7TF, England): **Factor XIII Concentrate in the Long Term Management of Congenital Factor XIII Deficiency.** **(25)**

Congenital Factor XIII deficiency causes a serious and disabling bleeding diathesis with a high risk of fatal intracranial haemorrhage. Blood levels of Factor XIII of a few percent of normal are sufficient to control bleeding and the in vivo half-life of Factor XIII is long, making permanent prophylaxis practicable.