

VAN DIE REDAKSIE

EDITORIAL

Tussentydse Kongres: Obstetrie en Ginekologie

Die 7de tussentydse Kongres van die Suid-Afrikaanse Vereniging van Verloskundiges en Ginekoloë vind plaas vanaf 30 September tot 3 Oktober 1974. Die vergaderplek is die Carlton Hotel in Johannesburg, en te oordeel na die program gaan hierdie 'n byeenkoms van besondere belang en interessantheid wees. Soos gewoonlik is verskeie buitelandse sprekers genooi om referate te lewer en vir die eerste keer, sover ons kon vasstel, word voorsiening gemaak vir gelyktydige vertaling van die verrigtinge in beide amptelike landstale. Dit is aangenaam om

dit te kan aankondig, want die gebrek aan Afrikaans by ons kongresse het dikwels in die verlede aanleiding gegee tot geregverdigde kritiek. Die teenwoordigheid van buitelanders het die gebruik van Afrikaans onprakties gemaak, veral gedurende ope besprekings, en vertalingsgeriewe is duur. Daarom sien ons veral uit daarna om die praktiese effekte van die vertalingdiens by hierdie tussentydse kongres te beleef. Indien dit suksesvol is, is dit te hope dat ander groepe die goeie voorbeeld sal kan volg.

Factor VIII, Haemophilia and Von Willebrand's Disease

Three distinct hereditary diseases have been described in which factor VIII function is deficient in plasma, namely classic haemophilia, von Willebrand's disease, and combined factor VIII and factor V deficiency.

The application of immunochemical, sucrose density ultracentrifugation and agarose gel filtration methods, has led to new concepts on the nature of factor VIII, haemophilia and von Willebrand's disease, as well as to the more accurate detection of carriers of haemophilia.

The factor VIII molecule appears to consist of multiple subunits which are associated by weak chemical interactions. Both low molecular weight (LMW) and high molecular weight (HMW) subunits are described, each with distinctive properties. The HMW subunits are coded at loci on autosomal chromosomes, have no coagulant activity, react with rabbit anti-factor VIII antibody, are present in normal or increased amounts in haemophilic plasma, and are decreased or absent in von Willebrand's plasma. They are also responsible for normal plate-

let stickiness and are attached to the endothelial cell. They have also been termed the factor VIII-related antigen. The LMW subunits are coded on the X chromosomes, and are assumed to contain the active coagulant sites of the factor VIII molecule. These LMW subunits are inactivated by antibodies produced in humans or rabbits, are not detected by immunoprecipitation or radio-immunoassay techniques, and do not precipitate with 25% saturated ammonium sulphate. They are not produced in haemophilia, and are usually decreased in direct proportion to the HMW subunits in von Willebrand's disease. The HMW subunits may be necessary to stimulate normal formation of the LMW subunits, which are then complexed with or carried within the HMW subunits. The coagulant activity of the LMW subunits may be unstable unless complexed with the HMW subunits. Therefore, in von Willebrand's disease, where there is a deficiency of the HMW subunits, there is usually a corresponding decrease in coagulant activity as well.

Transfusion of antihaemophilic factor to haemophilic patients results in an immediate increase in concentration of this factor (LMW subunits) to a predictable level. This concentration of LMW falls rapidly—half of the material disappearing within 12 hours. In contrast, in patients with von Willebrand's disease, the concentration of antihaemophilic factor (LMW subunits) continues to rise for 6 to 8 hours, to levels far beyond those predicted by the amount of antihaemophilic factor transfused. Thereafter the level of antihaemophilic factor (LMW) in the patient's plasma falls, but at a much slower rate than in classic haemophilia. The HMW subunits return to pre-infusion levels more rapidly than the LMW subunits.

Several patients have been described with von Willebrand's disease, in which the HMW subunit

concentration has differed significantly from that of the LMW subunits, suggesting the existence of variants of von Willebrand's disease.

The concepts emerging of the nature of haemophilia and von Willebrand's disease, therefore, are as follows: haemophilia is due either to failure of, or to defective synthesis of the LMW subunits of the factor VIII molecule, whereas the HMW subunits are produced normally. Von Willebrand's disease is due to reduced or defective synthesis of the HMW subunits of factor VIII. In most cases of von Willebrand's disease, the LMW subunits are reduced as well because the HMW subunits are required for their synthesis or release.

The application of these newer techniques and knowledge has made an important practical contribution to the detection of female carriers of haemophilia. Studies using rabbit anti-factor VIII antibodies have shown the presence of factor VIII-related antigen (HMW) in excess of factor VIII biological activity (LMW) in 95% of carriers. This increase in the ratio of HMW:LMW subunits is maintained in carriers even during periods of stress, such as pregnancy or exercise, when functional factor VIII levels may be within or above the normal range. The implications of this diagnostic bonanza for females who have the possibility of being carriers, need not be elaborated, as up to now the techniques available have been far less reliable.

Exciting new vistas continue to be developed in the field of haemophilia, a disorder known for thousands of years. With the new insight into the nature of the factor VIII molecule, as well as the interrelationships of haemophilia and von Willebrand's disease, the goal of genetic manipulation and of possible cure of these disorders does not seem an impossible dream.