SPECIAL REPORTS

Inhibitor Study Carrier Detection

PRELIMINARY REPORT OF THE COOPERATIVE STUDY OF SPONTANEOUSLY OCCURRING FACTOR VIII INHIBITORS IN PATIENTS WITH HEMOPHILIA. S. S. Shapiro, Cardeza Foundation for Hematologic Research, Department of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania, U.S.A.

A cooperative study was started in July 1975, sponsored by the Division of Blood Diseases, National Heart, Lung and Blood Institute, National Institutes of Health. The study includes 11 cooperating Centers throughout the United States as well as a computer center. All patients with Factor VIII coagulant levels below 0.10 u/ml (or even higher, if transfused often) are eligible for entry. Currently more than 1200 patients have been entered, including more than 200 with Factor VIII inhibitors. General information concerning the natural history of hemophilia is being collected, including a comparison of severity assessed clinically and in the laboratory, the incidence and degree of liver dysfunction, HB_sAg positivity, and hypertension. More than 200 patients with Factor VIII inhibitors have been identified, falling clearly into categories of "strong" and "weak" antibody producers. More than 200 treatment episodes have been documented in inhibitor patients, over 100 treated with Factor VIII and an equal number treated with Factor IX concentrates. Among the latter, some 20% have resulted in secondary rises in Factor VIII antibody titer. A controlled, blinded study of the efficacy of several Factor IX concentrates will begin shortly, and should be completed within a year.

CLASSIFYING POTENTIAL CARRIERS OF HEMOPHILIA: REPORT OF THE JOINT WFH-WHO EXPERT COMMITTEE. John B. Graham, University of North Carolina at Chapel Hill, North Carolina, USA.

The World Federation of Hemophilia and the World Health Organization convened an expert committee in Geneva, in Nov. 1976 to write a technical report on "carrier detection" in hemophilia. The committee consisted of: L.M. Aledort (USA), A.G. Bulanov (WHO), R.C. Elston (USA), E.K. Ginter (USSR), J.B. Graham (USA), J. Hermans (Neth), M.J. Larrieu (France), A.D. McLaren (UK), P.M. Mannucci (Italy), C.R.M. Prentice (UK), J.J. Velkamp (Neth). It attempted to prepare a technical report which would cover all aspects of the matter, yet be useful to non-experts. Laboratory methods were described in moderate detail, but major emphasis was placed on methods of genetic and statistical analysis, since these are less accessible to hematologists. It was suggested that help from a biostatistician is usually necessary at the start. Once statistical methods are well in hand, however, the personnel of a coagulation lab can manage the routine calculations. Methods were suggested for choosing and testing the validity of reference populations of carriers and controls, for estimating the number of "possible carriers" in a population. The logical imperative of incorporating the "likelihood ratio" obtained from the laboratory with the "prior probability" obtained from the pedigree was stressed; methods for calculating prior probabilities and incorporating linkage information were also described. Finally, it was emphasized that genetic counseling consists of more than merely offering a consultant the probabilities favoring carriership; it involves giving counsel to a family about all aspects of hemophilia.