Research in Haemophilia

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Research in haemophilia includes two different aspects, namely (1) basic research and (2) clinical research. Basic research on the immunology or biochemistry of the anti-haemophilic factors, Factors VIII and IX is performed in basic science laboratories. Such laboratories may be associated or closely related to International Haemophilia Training Centers (IHTC). Since basic research is essential for the further development of haemophilia care, information coming from these laboratories must be collected both by the World Federation of Hemophilia (WFH) and by National Societies.

Basic research over the last 5 years has been mainly devoted to the purification and characterization of antihaemophilic factors. Recent discoveries have had a definite impact on clinical research and haemophilia care. This can be illustrated by two examples: in 1980, Vehar and Davie [1] reported the purification from bovine plasma of the protein which carries the Factor VIII coagulant activity (VIII:C) which is lacking in haemophilia. This low molecular weight protein has been separated from the Von Willebrand factor, although they are always closely associated, and found in concentrates used for the treatment of haemophilia. If such a method allows the purification of pure human VIII:C, this will raise the question of the in vitro stability and the in vivo survival of this protein devoid of Von Willebrand factor.

An immunoradiometric assay of VIII Coagulant Antigen (VIII:CAg) was simultaneously described in 1978 by Lazarick and Hoyer [2] and Peake and Bloom [3, 4]. This assay allows the quantitative measurement of the antigen associated with the coagulant activity absent or decreased in haemophilia. It has numerous applications including the study of the heterogeneity of haemophilia A; prenatal diagnosis of haemophilia A, detection of haemophilia A carriers; and characterization of concentrates used for the treatment of haemophilia A.

Clinical research must result from a close cooperation between primary or comprehensive haemophilia centers, affiliated centers and haemophiliacs. Its aim is the improvement of haemophilia care and its objectives include different aspects such as new methods for the diagnosis, genetic counselling, substitution therapy and treatment of patients with inhibitors. Some of the questions raised about haemophilia may find an answer locally in a comprehensive center. However, most of the prospective trials require a multicenter study at a national or international level as shown in figure 1. Data collected from

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Cooperating centers

Patients Patients Patients Patients

Fig. 1. Proposed schema for a multicenter study.

Table I. Proposal for multicenter studies

Carrier detection Haemophilia A: VIII: CAg assay? Haemophilia B: F. IX and IX antigen

Substitution therapy Dosage requirements Low dose or high dose? Prophylactic treatment Low dose or high dose? Intervals?

Side effects

Incidence of hepatitis A, B, non-A, non-B

Liver function (liver biopsy?)

Short-term

Long-term effect

3 Treatment of patients with inhibitors Effect of plasmapheresis Nonactivated IX concentrates Versus activated IX concentrates

Clinical efficiency

Side effects

Immune response

Porcine F.VIII devoid of platelet-aggregating activity (FW)

cooperating centers with a variable number of patients are sent to a coordinating center which can be, for some objectives, closely associated with a reference laboratory. These multicenter studies may allow collection and control of laboratory data such as incidence of inhibitors occurring in haemophilia A and B and frequency of the different forms of hepatitis after multiple transfusions. They may also provide more rapid information about new therapeutic approaches such as the use of prothrombin complex concentrates in haemophiliacs with antibodies to factors VIII as recently reported by the haemophilia study group in United States [5].

A tentative list of proposals for multi-center studies at different levels is suggested in table I. Carrier detection, substitution therapy and treatment of patients with inhibitors remain at the present time the main objectives of clinical research in haemophilia.

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