

AHCDC von Willebrand Disease Scientific Sub-Committee

Annual Report 2005-2006

Members

David Lillicrap (Chairperson)
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Activities:

- a) The molecular basis of Type 1 VWD
- b) Quality of life assessment in VWD
- c) Observational study of DDAVP in VWD
- d) Von Willebrand disease in pregnancy
- e) The genetics of type 3 VWD
- f) Prophylactic therapy for VWD

A. The molecular basis of type 1 VWD (PI. David Lillicrap)

The Canadian type 1 VWD study has now completed recruitment and analysis of 150 families. The study has involved initial genetic linkage and association analysis the results of which are in press in the Journal of Thrombosis and Haemostasis. Subsequent to the linkage and association studies, which showed linkage to the VWF gene in just 40% of families, detailed sequencing of the VWF gene has been performed in 123 type 1 VWD index cases. In these most recent studies, that have juts been submitted to the journal Blood for review, a large amount of novel data has been derived relating to the complex genetic pathology underlying this condition. Further more mechanistic studies are now underway as part of a NIH-funded program project grant with investigators in Milwaukee (Drs Montgomery and Haberlichter) and Sheffield (Drs Goodeve and Peake).

B. Quality of life assessment in VWD (PI Ronnie Barr)

This multicenter study evaluating the influence of VWD on QoL will soon be closing recruitment. Standardized and validated QoL questionnaires have been completed by a large VWD population and correlated with the patients' Hb and serum ferritin levels. An abstract describing current progress with the study will be presented by the group from McMaster at the WFH meeting in Vancouver.

C. Observational studies of DDAVP in VWD (PI Augusto Federici)

This study has been organized by the VWF Scientific Subcommittee of the ISTH. Two Canadian centers, Toronto (HSC) and Kingston, have obtained IRB approval for the study and have begun recruiting patients. The goal is to contribute 10-15 patients into this two part international study.

D. Von Willebrand Disease in Pregnancy (PI Christine Demers)

This study is co-sponsored with the Women's bleeding disorder sub-committee. The aim of the study is to characterize the levels of VWF and FVIII in normal women and women with VWD during and immediately after pregnancy. Post-partum blood loss is also being quantified through validated methods. This study is now being supported by the Canadian Hemophilia Society.

E. The Genetics of type 3 VWD (PI Paula James)

This CHS-sponsored study has begun to enroll "nuclear trios" from families with type 3 VWD. The causative mutations in these families are being investigated and compared to the spectrum of mutations already documented in the Canadian type 1 VWD population. Correlations will also be made with evidence of anti-VWF alloantibody development.

F. Prophylactic treatment of VWD (PIs Berntorp and Abshire)

Discussions are ongoing with regards to a new international multicenter study of prophylactic therapy in patients with VWD that experience recurrent mucocutaneous or musculoskeletal bleeding. The AHCDC has been represented in these discussions by Drs Carcao and Winikoff. A consensus treatment protocol will likely be available shortly and it is anticipated that Canada will contribute patients to this study.