AHCDC VWD Committee – Annual Report 2013

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Activities

1. Development and approval of Terms of Reference
2. VWD and Angiodysplasia
3. Quantitative Assessments of Bleeding
4. Molecular Genetic Basis of VWD
5. Canadian VWD Guidelines

1. Terms of Reference

Terms of reference for all subcommittees were developed and reviewed this year. The ToR for the VWD subcommittee is attached to this report.

2. VWD and Angiodysplasia

The subcommittee has discussed and initiated plans for a national study evaluating the important problem of GI bleeding caused by angiodysplasia in VWD patients. A clinic survey, and registry project are in the development stage, with Drs. Natalia Rydz and Dawn Goodyear from the University of Calgary acting as P.I.s. This study will be complementary to lab-based studies taking place at Queen's University, led by Dr. James, evaluating the role of VWF in angiogenesis using BOEC (Blood Outgrowth Endothelial Cells) from VWD patients. An abstract describing preliminary data has been submitted to the ISTH SSC meeting being held in Milwaukee in June 2014, showing that Type 2B VWD BOEC exhibit increased angiogenesis when compared with normal and that the addition of atorvastatin to the cell culture media decreases vascularization.

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3. Quantitative Assessments of Bleeding

The primary focus of this research in the past year has been on self/parent-administered bleeding assessment tools. An adult study is being completed in Kingston, and will be presented at WFH in Melbourne in May 2014. This study is funded by an Investigator Initiated Grant from CSL Behring. The preliminary results show that the Self-BAT performs very well as a screening tool when used for females referred for the first time to Hematology for assessment of a possible bleeding disorder. In 22 subjects, a positive bleeding score as determined by the Self-BAT had a sensitivity=100%, specificity=18%, positive predictive value=0.26, negative predictive value=1.0 for the diagnosis of VWD. A companion pediatric study is also well underway, funded by a C17 Research Operating Grant. Drs. James and Rand are leading the study, with participation of Dr. Mariana Silva, Dr. Victor Blanchette, Dr. John Wu, Dr. Mac Steele, Dr. Sara Israels, Dr. Anthony Chan, Dr. Rob Klaassen, Dr. Vicky Price and Dr. Paul Moorehead. An abstract describing data comparing children known to have Type 1 VWD and normal children has been submitted to the ISTH SSC Milwaukee meeting, and the study is currently recruiting first time referrals to a Hematologist and testing the Self-PBQ as a screening tool for a bleeding disorder in that setting.

4. Molecular Genetic Basis of VWD

The research group at Queen's University, led by Drs. David Lillicrap and Paula James continues to be actively involved in projects evaluating the molecular genetic basis of VWD. Recent focus has included evaluation of the role of genetic loci outside of the *VWF* gene on VWF and FVIII levels, including CLEC4M, SCARA5 and STAB-2. Additional studies are focused on understanding the role of VWF propeptide mutations in Type 3 VWD, following up on the observation made during the Canadian Type 3 VWD Study that Type 3 VWD patients with propeptide mutations have higher bleeding scores than individuals with mutations elsewhere in the VWF gene.

5. Canadian VWD Guidelines

The VWD Subcommittee is keen to review and update our national VWD guidelines within the next 1 – 2 years. Discussions are underway about the best way to accomplish this.