AN INTRODUCTION TO VW DISEASE

Von-Willebrands Disease is a common inherited condition that can make patients bleed more easily than normal. There are 3 subtypesdue to either the lack of or reduced effectiveness of Von-Willebrand's factor, a blood protein that aids the formation of blood clots. It affects both men and women.

Von –Willebrand Factor (VWF)is a large plasma protein derived from vascular endothelial cells (also produced by megakaryocytes). It is stored in Wiebel Palade bodies in endothelial cells - some is released constitutively, some stored and released during inflammatory / traumatic stimuli. (VWF) is rapidly released in response to thrombin, adrenaline, histamine and vasopressin.

2 functions of VWF:

1. Binds to collagen at site of vascular injury and then captures platelets to form haemostatic plug.
2. Stabilises Factor VIII in circulation and maintains functionality.

FVIII and VWF circulate together as a complex in which VWF protects FVIII from degradation – so low VWF / inability to bind FVIII will deplete FVIII also. VWF is released into circulation in large multimers (very adhesive to collagen and platelets) which are cleaved into smaller molecules by the metalloprotease ADAMTS13. Absence,deficiency or immune destruction of ADAMTS13 may lead to micro-thrombi production as seen in thrombotic thrombovytopenic purpura (TTP).

Clinical Features of VWD – vary according to severity of the deficiency. Most commonly: mild to moderately severe bleeding tendency characterised by bruising, epistaxis, menorrhagia and excessive (not often life-threatening) bleeding after surgery. The history is key – prolonged bleeding / transfusion / return to surgery after haemostatic challenges such as dental extraction, menstruation, surgery, child-birth are good indicators of a problem.

Diagnosis –

- Obtain a bleeding history and family – this is the most important step!
- This is usually muco-cutaneous or menorrhagia.

- The phenotype does not always align with reduced VWF assays. Persons can have reduced levels yet no bleeding history
- Quantification of VWF present in plasma (VWF:Ag)
- Platelet-dependent function of VWF – (VWF:RCo) dilutions of patients platelet-rich plasma are tested for their ability to promote platelet agglutination in the presence of the antibiotic ristocetin.
- FVIII binding (VWF:FVIIIB) – assessed by quantity of FVIII in plasma, can go on to do an ELISA based assay with wells coated in FVIII.
- Collagen binding function (VWF:CB) – ELISA based technique using wells coated with collagen.
- Multimer quantification
- RIPA – "normal" washed platelets are added to patients platelet-poor plasma before addition of ristocetin – to prove the problem is with the patients VWF not their platelets – useful to identify type 2B VWD.

Type 1 VWD – most common – a simple quantitative deficiency of VWF but the VWF present is functionally normal with normal multimers. The ratio of VWF:RCo/VWF:Ag should be >0.6.

Type 2 VWD – a functional qualitative defect of VWF activity

Type 3

This is more severe, generally due to compound genetics, ie 2 abnormal parental genes and so with some joint bleeding similar to Moderate Haemophilia

Table 1. Classification of von Willebrand Disease

Type	Description
1	Partial quantitative deficiency of VWF
2	Qualitative VWF defects
2A	Decreased VWF-dependent platelet adhesion with deficiency of HMW multimers
2B	Increased affinity for platelet GPIbα
2M	Decreased VWF-dependent platelet adhesion with a normal multimer distribution
2N	Decreased VWF binding affinity for FVIII
3	Virtually complete deficiency of VWF

FVIII, factor VIII; HMW, high-molecular-weight; VWF, von Willebrand factor.

Treatment

- Assess bleed or type of surgical intervention

Type 1

- Commonly desmopressin (pharmaceutical vasopressin) SC or IV (usual dose is 0.3mcg/kg), if given sc use Octim (15cg/ml) takes 90 mins to reach peak effectiveness.
- For very minor injury or procedure - simply tranexamic acid (oral or IV), usual adult dose 1g TDS for 5-10days

Types 2 and 3

- Some type 2A's may respond to demospressin
- Otherwise factor therapy (intermediate purity factor VIII containing vWF, or recombinant vWF)
- Tranexamic acid for minor bleeds