We particularly studied the varied & unvalidated antenatal management of VTE in the UK rather than postpartum treatment, which uses the well-established regimens used in the non-pregnant patient.

The optimal low molecular weight heparin (LMWH) dosing regimen in pregnancy has not been clearly established. Collectively, the two studies showed wide variability in treatment schedules between and within centres, without any evidence for superiority of one regime over another. The practice of dose reduction also varied widely. In selected Nottingham patients, the conversion to once daily dose as pregnancy advanced appeared to be safe and effective, as it was in the 22% of mothers who received this treatment in our study. Once daily injections (as used in non-pregnant patients and given to a minority of the Nottingham antenatal patients and to 66% in our study) appears to be a safe and popular option for women with calf deep vein thrombosis or those in whom there has been clinical resolution of symptoms after several weeks of twice daily injections. These findings raise the possibility that this more convenient regimen could have wider application in the treatment of VTE in pregnancy. However this needs to be tested in an appropriately powered randomised case controlled study.

The noted risk factors emphasised the importance of thrombophilia, family history and previous venous thromboembolic disease. The relatively low number of patients on thromboprophylaxis in both surveys suggest a failure of effective antenatal screening and appropriate referral. Both studies noted that a proportion of women who failed thromboprophylaxis were on low doses. This provides some validation of the dosing regimen currently recommended by the Royal College of Obstetricians and Gynaecologists (RCOG 2004).

Our study found poor documentation of dose and timing of peripartum anticoagulation. This was better in Lyall & Myers' study, perhaps reflecting more consistent record keeping in a single centre. The implication is that improvements in record keeping are needed and can be achieved, to ensure safe delivery and reduce the risk of early postpartum haemorrhage. Full anticoagulation within the first few days, particularly with early transfer to warfarin, increased the risk of postpartum haemorrhage in both studies, suggesting that transfer to warfarin should be delayed for 1–4 weeks.

In the absence of large case controlled or comparative antenatal studies, surveys, such as ours (Voke *et al*, 2007) and that of Lyall & Myers, provide a valuable contribution to our understanding of risk factors and management of VTE in pregnancy.

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Differential identification of PT-VWD from type 2B VWD and GP1BA nomenclature issues

I read with interest the recent letter by Favaloro *et al* (2007), reporting that a simplified ristocetin-induced-platelet-agglutination (RIPA) mixing assay correctly identified three platelet type von Willebrand disease (PT-VWD) individuals in which the phenotype was later confirmed by genetic analysis. Although we should await responses from other hemostasis laboratories following the implementation of the assay in their laboratory, this assay has superiority over the cryoprecipitate challenge and standard RIPA because it provides simultaneous answers regarding the two disorders. Undoubtedly, the genetic approach supported by us and others (Whalley & Perry, 2007; Favaloro, 2008) remains the gold standard for identifying the

Table I. Nomenclature and numbering related to known *GP1BA* mutations and polymorphisms.

	Nucleotide number		Amino acid number	
Common name in literature	Conventional # (G at TSS as +1)	New # (A of ATG as +1)	Conventional # (H as +1)	New # (M as +1)
GP1BA mutations				
Gly233Val	G>T 788	G>T 746	Gly233Val	Gly249Val
Gly233Ser	G>A 788	G>A 746	Gly233Ser	Gly249Ser
Met239Val	A>G 805	A>G 763	Met239Val	Met255Val
27 bp del	1348 del 27	1306 del 27	420–428 del 9	436–444 del 9
GP1BA polymorphisms				
Kozak	−5 T>C	−5 T>C	NA	NA
Leu70Phe	C>T 298	C>T 256	Leu70 Phe	Leu86Phe
Thr145Met	C>T 524	C>T 482	Thr145Met	Thr161Met
VNTR D allele: 1 repeat	1285–1324	1243–1282	399–412	415–428
VNTR C allele: 2 repeats	1285–1363	1243–1321	399–425	415–441
VNTR B allele: 3 repeats	1285–1402	1243–1360	399–438	415–454
VNTR A allele: 4 repeats	1285–1441	1243–1399	399–451	415–467

gene mutation in *VWF* vs. platelet *GP1BA* genes. Furthermore, the potential misdiagnosis of PT-VWD as 2B VWD can only be revealed with large molecular studies. We recently proposed an international PT-VWD project and also called for a PT-VWD online database/disease registry (Othman, 2007; Othman & Lillicrap, 2007) to help address questions related to this diagnostic dilemma; the latter is now available at http://www.pt-vwd.org.

Favaloro *et al* (2007) referred to the previously reported Gly233 Ser as Gly246Ser. This raises a critical point about the nucleotide and amino-acid (aa) numbering of *GP1BA* as well as mutation description. The human gene nomenclature committee (HGNC) (http://www.genenames.org/) that stems from the human genome organisation (HUGO) and the affiliated human genome variation society (HGVS) (http://www.hgvs.org/) recommend that nucleotide numbering should start at the ATG translation codon and all nucleotides upstream of this A should be numbered as −1 and the aa numbering should start from the first Met of the polypeptide chain. The *GP1BA* cloned in 1987 (Lopez *et al*, 1987) consists of two exons with 42 nucleotides of 5′ non-coding sequence. The entire coding sequence is contained within exon 2, the first 48 nucleotides of exon 2 codes for a 16 aa signal peptide and the mature protein starts at aa His. Accordingly, the PT-VWD mutation historically known as 788 G>A; Gly 233 Ser should ideally be referred to as the 746 G>A; Gly 249 Ser, as described by Favaloro *et al* (2007). Likewise, other *GP1BA* mutations/polymorphisms will have different nomenclature, as shown in Table I. Regarding the name of the platelet gene/protein, we support the name *GP1BA* (1 arabic numeral instead of Latin) as listed for this gene in the HGNC website (ID:4439), italicised when referring to the gene and non italicised when referring to the protein.

Similarly, in the *VWF* gene, different Investigators have used different mutation nomenclature based on whether numbering starts from the first Met or the first aa of the mature protein (Ser 763) which have sometimes created confusion. Examples are: Cys 1149 Arg (Cys 386 Arg) and Cys 1130 phe (Cys 367 Phe), Type 1 Malmo/New york (Weiss & Sussman, 1986) Pro1266 Leu (Pro 504 Leu). It is worth noting that two recently reported type 1 VWD studies (Goodeve *et al*, 2007; James *et al*, 2007) have followed the standard nomenclature and that the VWD database (http://www.vwf.group.shef.ac.uk/) has been updated to accommodate the new nomenclature.

Following a standard nomenclature is critically important for consistent description of gene sequence variations in order to reduce the confusion among clinicians and researchers regarding the diagnosis of genetic disorders. However, we realize it takes effort and great deal of awareness to consistently implement this nomenclature universally.

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Differential identification of PT-VWD from type 2B VWD and *GP1BA* nomenclature issues response to Othman

We thank Dr Othman for her interest in our recent communication (Favaloro *et al*, 2007). We would entirely agree that genetic testing remains the gold standard for the differential diagnosis of type 2B von Willebrand disease (VWD) and platelet-type (PT, 'pseudo') VWD, and are in full support of the proposed PT-VWD online database/disease registry (http://www.pt-vwd.org) plus future planned projects in this important area of clinical investigation (Othman, 2007; Othman & Lillicrap, 2007). We also agree that a standard nomenclature is critically important for the consistent description of gene sequence variation and for reducing the potential for confusion for workers in the field.

Nevertheless, we reiterate the importance of appropriate phenotypic testing to help identify and provisionally classify such patients for subsequent genetic study, since (i) it is doubtful that the latter will progress without an informative preliminary phenotypic workup and (ii) an appropriate phenotypic workup will guide the genetic investigation (i.e. whether to focus on *VWF* or *GP1BA*). Furthermore, since such individuals appear to vary widely in terms of their phenotypic presentation (Favaloro, 2008), the specific selection of the most appropriate phenotypic tests or test panels may be more important than previously recognized. An inappropriate selection will result in these patients otherwise being misdiagnosed or their identification will be missed altogether. It is also possible that the classical phenotypic testing approach may no longer be sufficient. For example, a recent report (Casonato *et al*, 2007) has identified an unusual case of type 2B-like VWD, which was characterized by enhanced ristocetin-induced platelet aggregation (RIPA) and a mutation in *VWF*, but without evident loss of plasma von Willbrand factor *per se*. It would seem feasible that similar cases of PT-VWD might also arise.

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