The role of PFA-100® testing in the investigation and management of haemostatic defects in children and adults

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Summary

The PFA-100® provides a simple global measure of high shear-dependent platelet function, and as such is not diagnostic or specific to any disorder. Prolonged closure times must be interpreted in conjunction with a full blood count, von Willebrand factor (VWF) screen and other platelet tests. The PFA-100® may also give false negative results with relatively common platelet defects. If clinical suspicion is high, further detailed platelet function testing and VWF screening are required to exclude abnormal platelet function, even if the PFA-100® is normal. In more recent studies the PFA-100® has been used for preoperative identification and management of surgical patients with haemostatic defects and for assessing the clinical effectiveness of platelet transfusion therapy. This review highlights the up to date, evidence-based, advantages and disadvantages of the PFA-100® test in the investigation and management of haemostatic disorders in both children and adults.

Keywords: PFA-100®, platelet function testing, aggregometry, bleeding time, high shear.

Current platelet function tests are labour intensive, time consuming and require a fair degree of expertise to perform and interpret, e.g. aggregation tracings. Since the last British Committee for Standards in Haematology (BCSH) guidelines for platelet function testing were published (British Society for Haematology BCSH Haemostasis and Thrombosis Task Force, 1988), there have been considerable advances with the availability of new platelet function tests including the development of a range of global instruments/tests that attempt to simulate in vivo platelet adhesion and aggregation (Harrison, 2000, 2005; Rand et al, 2003). One of these tests, 'the thrombostat 4000', was developed in 1985 in an attempt to simulate high shear-dependent platelet adhesion and aggregation to collagen-coated surfaces (Kratzer & Born, 1985). In the mid-1990’s, Dade-Behring (Marburg, Germany) further refined the test into a commercially available instrument called the platelet function analyser or PFA-100® (Kundu et al, 1995; Jilma, 2001; Francis, 2004). The instrument utilizes test cartridges that contain a collagen/ADP (CADP) or collagen/epinephrine (CEPI) coated membrane with a small central aperture (147 μm). Citrated blood is aspirated under high shear (5000–6000/s) from the sample reservoir through a capillary tube onto the membrane and blood flow is monitored through the aperture. Platelets begin to adhere and aggregate, primarily via von Willebrand factor (VWF) interactions with glycoprotein (Gp)Ib and GpIIb/IIIa, resulting in occlusion of the aperture normally between 1 and 3 min from test initiation. The instrument simply monitors the drop in flow rate with time as the aperture gradually occludes and records the final closure time (CT) and volume of blood that has been aspirated through the aperture. Maximal CTs are 5 min and the instrument will give a result >300 s if this time is exceeded. PFA-100® testing is relatively simple, rapid and easy to learn. However, there are some recently published detailed guidelines/procedures that can help to ensure optimal performance (Harrison, 2004). These include daily quality control checks, quality of anticoagulation and blood sampling, establishing local normal ranges and controlling for possible cartridge batch variation (Bock et al, 1999; Harrison, 2004). Various recent articles have highlighted the remarkably similar published normal ranges for both CADP and CEPI cartridges, within either 3.2% or 3.8% citrated blood, reported from many laboratories (Favaloro et al, 1999; Favaloro, 2001; Jilma, 2001). This adds to the growing evidence that suggests that the test is reproducible both between cartridge lots and instruments. However, despite good inter-laboratory agreement, each test centre should also ideally establish their own normal reference ranges on both cartridges utilizing normal volunteers (Harrison, 2004). Intra-sample reproducibility has been reported to be approximately 10%, which, although probably acceptable for a test of this type, may cause problems in the interpretation of values close to the upper cutoff of normal ranges (Harrison et al, 1999).

Variables that influence the PFA-100

The PFA-100® is a global test of high shear-dependent platelet adhesion and aggregation. The test is, therefore, sensitive to a
large number of variables that are also known to affect platelet function *in vivo* (Kundu *et al*, 1996; Harrison *et al*, 1999). The PFA-100® is sensitive to platelet count, haematocrit, drug effects, dietary effects, major platelet receptor defects, VWF defects, release defects and granular defects (Kundu *et al*, 1996; Fressinaud *et al*, 1998; Mammen *et al*, 1998; Cattaneo *et al*, 1999a,b; Harrison *et al*, 1999; Jilma, 2001). Testing should always be performed with knowledge of the full blood count, as platelet counts and haematocrits below $<80 \times 10^9/l$ or $<30\%$ respectively often result in prolongation of the CT (Kundu *et al*, 1995; Harrison *et al*, 1999; Jilma, 2001). Citrate samples have been shown to be stable for up to 5–6 h (<4 h recommended by Dade-Behring) after collection for PFA-100® testing (Harrison *et al*, 1999), but transport through a vacuum transport system is not recommended prior to analysis as this may influence the results (Dyszkiewicz-Korpan *et al*, 2004). As the PFA-100® is a high shear system, plasma and platelet levels of VWF are very important in determining a normal CT (Fressinaud *et al*, 1998, 1999). There is a strong inverse correlation between PFA-100® CTs and plasma VWF levels. ABO blood groups, therefore, also influence the PFA-100®, although CTs are usually in the normal range (Moeller *et al*, 2001). Not surprisingly, the test has, therefore, been reported to be very sensitive to all subtypes of von Willebrand disease (VWD) (except type IIN, where there is defect in the Factor VIII binding capacity of VWF but not in platelet function) (Fressinaud *et al*, 1998, 1999). Any significant defect in copy number or functionality of GpIb or GpIIb/IIIa also results in prolongation of CTs (Harrison *et al*, 1999, 2002a). Both collagen receptors GpIa/IIa and GPVI also seem to play a role in the direct activation and/or adhesion of platelets to the membrane (Di Paola *et al*, 1999; Best *et al*, 2003). The CEPI cartridge has also been reported to be more sensitive than the CADP cartridge at detecting storage and/or release defects in dense granular ADP and defects in thromboxane generation (e.g. caused by aspirin) (Cattaneo *et al*, 1999b; Harrison *et al*, 1999; Homoncik *et al*, 2000; Jilma, 2001). This suggests that the high concentration of ADP within the CADP cartridge is sensitive to many mild platelet defects and does not necessarily correlate with, or even predict, a bleeding tendency. An accurate bleeding history is, therefore, now considered as a more valuable screening test. The important question is, therefore, whether the same limitations apply to the PFA-100®, which is often considered as an *in vitro* equivalent of the BT. There have been a number of head-to-head comparisons of the PFA-100® with the BT. Early studies have shown the PFA-100® to be more sensitive to VWD, including type I VWD than the BT (Fressinaud *et al*, 1998; Cattaneo *et al*, 1999a; Favalaro *et al*, 1999; Dean *et al*, 2000). A direct comparison of the two tests with platelet defects in an unselected population demonstrated improved sensitivity of the PFA-100® over the BT and with a high degree of agreement with platelet aggregation (86%) (Francis *et al*, 1999). A more recent study also demonstrated that the PFA-100® was more sensitive than the BT to VWD and platelet defects in a paediatric population (Cariappa *et al*, 2003). Although the overall sensitivity of the PFA-100® to VWD seems to be excellent when compared with the BT, there have been reported differing sensitivities to type I VWD (Harrison *et al*, 2002a,b; Liesner *et al*, 2004; Quiroga *et al*, 2004a). Borderline VWF levels on either side of laboratory cut-offs can sometimes give normal or abnormal CTs. This is further complicated by the important roles of platelet VWF (which may be normal or abnormal), temporal variation in VWF levels (sometimes within the normal range), collagen receptor density [which can often be lower in type I VWD (Di Paola *et al*, 1999)] and blood groups, all of which affect the clinical phenotype and PFA-100® CTs. Type I VWD, therefore, remains a diagnostic challenge. The true performance and clinical relevance of the PFA-100® in type I VWD should be shortly revealed from the results of a large European Union multicentre study (MCMDM-1VWD). In this study, a clinical bleeding score will be compared with a phenotypic assessment including the PFA-100® and BT.

In patients with Hermansky–Pudlak syndrome the BT actually seemed slightly more sensitive than the PFA-100®
Although numbers studied were small (Kerenyi et al, 1999). A comparison of BT and PFA-100® in patients with congenital defects of platelet secretion [storage pool disease (SPD) and primary secretion defects (PSD)] showed that both tests performed similarly with low sensitivity (Cattaneo et al, 1999b). Given that a large number of platelet abnormalities encountered are PSD (Cattaneo, 2003), this represents a significant limitation of the PFA-100®. Perhaps the future availability of different agonists within new cartridges may help to improve the sensitivity of the PFA-100® to these type of disorders (Escolar et al, 2001). However, the CEPI cartridge is more sensitive than the CADP cartridge in detecting these type of disorders and has been recently shown to be significantly associated with the clinical bleeding score in 128 patients (Podda et al, 2005).

A more recent study demonstrated that the PFA-100® and BT were both relatively insensitive in 148 patients with unequivocal mucocutaneous bleeding and positive family history (Quiroga et al, 2004a). As expected the PFA-100® performed slightly better than the BT in patients with type 1 VWD (sensitivity 61.5% vs. 42%) but at a much lower sensitivity than previous studies (Quiroga et al, 2004a). However, the BT was actually slightly better than the PFA-100® in patients with PSD (sensitivity 42% vs. 24%) (Quiroga et al, 2004a). The main conclusion from the study is that use of the BT and PFA-100® in the diagnostic work up of these type of patients is not completely justified and that global screening tests (e.g. BT and PFA-100®) are therefore of limited utility (Cattaneo, 2004; Quiroga et al, 2004a). Therefore, one could argue that a clinician faced with an individual with a well defined personal and family history of mucocutaneous bleeding should therefore not use the results of a global screening test to influence their decision whether to undertake further specific platelet function tests (Cattaneo, 2004). However, the PFA-100® does have a high sensitivity to VWD and one could equally argue that it still offers the relative comfort of a rapid screening test well before VWF and other platelet function tests can all be performed to give an accurate diagnosis (Favaloro, 2004). The availability of new rapid and reliable automated VWF antigen and VWF activity assays may somewhat help to alleviate this problem by significantly decreasing the time delays before results are obtained. However, given the high negative predictive value of the PFA-100®, the test can be urgently utilized to exclude not only VWD but also severe but rare severe platelet defects, such at Glanzmann’s Thrombasthenia and Bernard Soulier (BS) disease, as these also give very prolonged CTs (Favaloro, 2004). As BS patients also present with macrothrombocytopenia, the CT is useful at discriminating this severe platelet defect from other thrombocytopenic conditions presenting with large platelets and similar counts (e.g. idiopathic thrombocytopenic purpura), as these often give normal CTs (Carcao et al, 2002). However, if the clinical suspicion is strong then specific tests must always still be performed even if the PFA-100® is normal (Cattaneo, 2004; Favaloro, 2004). Providing there is sufficient time to perform a comprehensive platelet function and VWF analysis then one could also argue that the PFA-100® may also be completely omitted from being used. Certain laboratories have therefore abandoned the use of the PFA-100® and the BT as a screening test because of these problems (Hajdenberg, 2004), although many laboratories still maintain the need for a global test of platelet function, mainly because clinicians historically request and like an urgent and instant test result (Quiroga et al, 2004b). The test may therefore be somewhat limited but still offers a rapid means to exclude the presence of VWD and the more severe forms of platelet disorders because of its high negative predictive value for these disorders (Favaloro, 2004). Of course, any false positive samples will also have to be fully tested with a panel of additional platelet function tests to eliminate any possibility of a platelet defect. Interestingly, the PFA-100® has been reported to potentially identify an unknown platelet defect(s) with consistently very prolonged CTs (>300 s) on both cartridges despite all other tests being normal in a small number of patients with well defined bleeding histories (Oxford Haemophilia Centre, unpublished observations and Doug Christie, personal communication). This suggests that the PFA-100® may identify as yet unknown defect(s) in shear-dependent platelet function.

The use of the PFA-100® for preoperative identification and management of patients with impaired haemostasis

Approximately 3–5% of patients undergoing surgery have either an acquired platelet defect, a congenital platelet defect or VWD. Could a preoperative screen with a test, such as the PFA-100®, therefore be beneficial to not only to potentially exclude them from surgery but also monitor any haemostatic therapy? A very recent large prospective study attempted to identify both primary and secondary haemostatic defects before surgery in 5649 unselected adult patients (Koscielny et al, 2004a). Each patient filled in a detailed questionnaire concerning bleeding history and a number of screening tests were performed including PFA-100® (CADP and CEPI cartridges), activated partial thromboplastin time, prothrombin time and platelet count. VWF and BT’s were additionally performed in those patients with a positive bleeding history and/or evidence of a haemostatic defect. The bleeding history was negative in 89% (n = 5021) of patients and positive in the remaining 11% (n = 628). Of these, impaired haemostasis was verified in 40.8% (n = 256). Interestingly, the CEPI cartridge identified 98% (n = 250) of these patients (sensitivity of 91%) while the CADP cartridge identified 78%. The overall sensitivity of the CEPI cartridge was the highest (91%) compared with all other screening tests. The positive predictive value of the CEPI cartridge was 82% with a negative predictive value of 93%. Therefore, the combined use of a standardized questionnaire and PFA-100® as a screening test were capable of detecting impaired haemostasis in almost every case (Koscielny et al, 2004a). As part of this study, patients with impaired
primary haemostasis were then treated with desmopressin (DDAVP) (Koscielny et al., 2004b). Non-responders, as defined by the PFA-100®, were additionally treated with tranexamic acid or aprotinin and in the cases with VWD, VWF-containing factor VIII concentrates. The treatment of DDAVP led to correction of PFA-100® CTs of 229 of 254 patients and tranexamic acid was effective in 12 of 16, aprotinin in three of five and factor VIII concentrates in four of four patients. If all of these treatments were ineffective then conjugated oestrogens (n = 6) were given and finally, as a last resort, platelet transfusions were given (n = 2). Interestingly, the frequency of blood transfusions was no different (9-4% vs. 12-2%, P = 0.202) in preoperative patients with impaired haemostasis than in patients without impaired haemostasis. In a retrospective study, the frequency of blood transfusions was significantly higher (89-3% vs. 11.3%, P < 0.001) in patients without preoperative correction of impaired haemostasis versus patients without impaired haemostasis (Koscielny et al., 2004b). This shows the potential of the PFA-100® not only as a preoperative screening test but for monitoring preoperative correction with pro-haemostatic agents (Koscielny et al., 2004a,b). The use of the PFA-100® in this setting may therefore potentially reduce the number of unnecessary blood transfusions. The key criticisms of this study are that the control group was from a retrospective study, that there was a control group was from a retrospective study, that there was a

**The use of the PFA-100® in a paediatric setting**

The evaluation of platelet function in children can be difficult. The ‘gold standard’ diagnostic tests of platelet function remain platelet aggregation and nucleotide measurements. These tests are usually only performed in well-equipped coagulation laboratories and are time consuming and often technically challenging. They also usually require a minimum of about 10–20 ml of blood, which can often be a significant problem in young infants. The BT is very difficult to perform in young infants because the test involves laceration of the forearm and the stress on parents, patients and clinical staff can be substantial as they attempt to restrain the child during the test (Cariappa et al, 2003). Standard template devices that have been used for BT measurement in Adults have been modified in for use in children and neonates so that the size of the incision is decreased (Feusner, 1980; Andrew et al, 1989). BTs have been reported to be longer in children than adults but shorter in newborn infants (Andrew et al, 1990; Sanders et al, 1990). This also raises the ethical issue of performing normal ranges for the BT in healthy children. However, all of the current criticisms of the BT remain (see above) (Rodgers & Levin, 1990; Lind, 2002; Francis, 2004), and moreover repeat and even single testing is often unacceptable to children and their families. Non-invasive tests, which utilize minimal quantities of blood, are therefore potentially very useful in this setting. Only a total of 1-6 ml of citrated blood is required to perform a PFA-100® test with both CADP and CEPI cartridges. PFA-100® normal ranges for children beyond the neonatal period have also been reported to be very similar to adults (Carcao et al, 1998; Jilma, 2001). However, blood from term neonates has been shown to exhibit shorter CTs than both older children and adults (Kottke-Marchant et al, 1999; Israel et al, 2001). The shorter CTs appear to correlate with raised Haematomics and increased VWF ristocetin cofactor activity due to the presence of ultra large VWF (Israel et al, 2001; Boudewijns et al, 2003). As normal ranges in older children are similar to adults, then the PFA-100® can be a very useful rapid test to exclude VWD and severe platelet defects, such as Glanzmann’s Thrombasthenia and BS disease. Three separate studies have evaluated the utility of the PFA-100® in a paediatric setting (Carcao et al, 1998; Dean et al, 2000; Cariappa et al, 2003). All concluded that the test is potentially useful in screening for VWD and is more sensitive than the BT. One study suggested that if PFA-100® testing was performed twice and the results were in the normal range on both occasions, then a full VWD work up is not required (Dean et al, 2000). Children with Haemophilia A and B were also shown to give normal PFA-100® results, confirming that the test is independent of coagulation (Carcao et al, 1998; Rand et al, 1998; Dean et al, 2000). More recent evidence suggests that the test is not completely sensitive for the detection of non-severe platelet defects in children, including some patients with type I VWD, dense granular defects, PSD (Liesner et al, 2004) and Hermansky Pudlak syndrome (Harrison et al, 2002b), results that parallel similar studies in adults.
PFA-100\textsuperscript{®} testing of paediatric samples may therefore provide some important information for the exclusion of VWD and severe platelet defects, especially where the availability of blood may be a limiting factor. The test may also help to exclude these disorders in cases of non-accidental injury (Liesner et al., 2004), although exclusion of other platelet defects with formal platelet function testing may also be necessary.

**Use of the PFA-100\textsuperscript{®} in monitoring haemostatic therapy**

The PFA-100\textsuperscript{®} seems to have utility for rapidly monitoring responses to DDAVP therapy (Cattaneo et al., 1999a; Fressinaud et al., 1999; Favaloro et al., 2001). As the test is sensitive to VWF level, DDAVP responses can be monitored because of the rapid release of the endothelial stored pool of endogenous high molecular weight (MW) VWF, resulting in a transient increase in the level of plasma VWF levels and increased proportion of high MW multimers. Patients with normal VWF and with type I VWD, therefore, usually respond very well to DDAVP, with shortening and/or normalization of CTs (Cattaneo et al., 1999a; Fressinaud et al., 1999; Favaloro et al., 2001). However, patients with some forms of type I and type IIA VWD were shown not to respond in their CTs as well, despite apparent correction of plasma VWF levels, presumably because of the role of intraplatelet VWF in platelet plug formation and/or the absence of high MW multimers.

### Table I. A list of Clinical Applications of the PFA-100 test. The major advantages and limitations of the test are shown for each individual application.

<table>
<thead>
<tr>
<th>Clinical application</th>
<th>Advantage</th>
<th>Limitation</th>
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<tbody>
<tr>
<td>(1) Replacing the BT as a screening tool</td>
<td>More sensitive and reliable than the BT. Rapid results</td>
<td>Results not diagnostic or specific</td>
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<tr>
<td></td>
<td>Easy test to perform</td>
<td>Inflexible fixed system, only two cartridges currently available</td>
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<tr>
<td></td>
<td>Non-invasive – requires only 0.8 ml of blood per cartridge</td>
<td>Requires buffered citrate samples</td>
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<td></td>
<td>Samples can be tested &lt;4 h old</td>
<td>Vacuum transport system for samples may affect test results</td>
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<td></td>
<td>High sensitivity to VWD and severe platelet defects</td>
<td>Low sensitivity to SPD, HPS, and PSD.</td>
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<td></td>
<td>CVs of normal samples &lt;10%</td>
<td>Some false negatives occur in type I VWD</td>
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<tr>
<td></td>
<td>Physiological test of high shear dependent platelet function</td>
<td>Interpretation of results near cut-offs. CVs are higher in abnormals</td>
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<td></td>
<td>High negative predictive value</td>
<td>No measure of vascular wall function</td>
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<td>(2) Monitoring pro-haemostatic therapy</td>
<td>Sensitive to DDAVP and release of endothelial VWF into the blood</td>
<td>False and true positives have to be diagnosed with a panel of tests. Also, if clinical suspicion is high and PFA is normal then other tests are still required</td>
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<tr>
<td></td>
<td>Can monitor platelet transfusions</td>
<td>Abnormal CTs can be frequently encountered. Retesting often required</td>
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<tr>
<td></td>
<td>Coagulation-independent</td>
<td>Sensitive to platelet VWF and high MW VWF.</td>
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<tr>
<td>(3) Monitoring anti-platelet therapy</td>
<td>Aspirin and NSAIDs usually prolong the CEPI CT</td>
<td>CTs do not always correct with VWF concentrates</td>
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<td></td>
<td></td>
<td>Often sensitive to platelet count</td>
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<tr>
<td>(4) Detecting and managing preoperative haemostatic defects</td>
<td>Can be used as a point-of-care test without a specialized laboratory</td>
<td>Insensitive to Factor VIIa</td>
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<td>(5) Screening women with menorrhagia</td>
<td>High incidence of VWD and platelet dysfunction.</td>
<td>Often insensitive to clopidogrel</td>
</tr>
<tr>
<td>(6) Screening platelet donors</td>
<td>High negative predictive value</td>
<td>Not diagnostic</td>
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<tr>
<td></td>
<td>Detection of both permanent and transiently acquired defects, e.g. aspirin.</td>
<td>Not diagnostic. No proof yet that transient drug/diet effects influence the haemostatic potential of concentrates</td>
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<td>Donors can be eliminated or deferred</td>
<td>Requires addition of RBC and plasma to the concentrates for testing</td>
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<tr>
<td>(7) Quality control of platelet concentrates</td>
<td>Monitor storage lesion</td>
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</table>

BT, bleeding time; VWD, von Willebrand disease; PSD, primary secretion defects; HPS, Hermansky-Pudlak syndrome; SPD, storage pool disease; CV, coefficient of variation; CT, closure time; PFA, platelet function analysis; DDAVP, desmopressin; VWF, von Willebrand factor; MW, molecular weight; NSAIDs, non-steroid anti-inflammatory drugs; CEPI, collagen/epinephrine; RBC, red blood cells.
The PFA-100® has also been utilized to monitor responses to VWF concentrate infusion in patients with DDAVP non-responsive type III and type IIA VWD. Disappointingly CTs tend not be normalized, probably because the concentrates are deficient in the highest MW multimers and/or that platelet VWF is absent in type III VWD (Cattaneo et al., 1999a; Fressinaud et al., 1999). The test therefore appears to have limited utility for monitoring VWF concentrate therapy. It will be interesting to determine whether future development and availability of fully multimeric VWF concentrates (e.g. recombinant VWF) may result in normalization of CTs postinfusion.

High dose factor VIIa infusion is now becoming increasingly useful for the treatment of platelet disorders. In our experience, factor VIIa does not influence CTs on the PFA-100® in children with platelet disorders (Almeida et al., 2003). Theoretically, as factor VIIa is increasing the amount of thrombin generation on the platelet surface, it is conceivable that the PFA-100® should be insensitive to this clotting factor, as the test is largely coagulation independent. It is likely that the test may not be useful for monitoring factor VIIa therapy. Koscielny et al. (2004b) also studied the utility of the PFA-100® in monitoring pro-haemostatic therapy in patients with impaired haemostasis. Interestingly, they concluded that the PFA-100® could be useful for monitoring not only DDAVP, but transexamic acid, aprotinin, oestrogen, platelet transfusion and even factor VIII concentrates (containing VWF) (Koscielny et al., 2004b).

**What can the PFA-100 be used for in clinical practice?**

The PFA-100 provides us with a unique test of high shear-dependent platelet function. Widespread experience with the test is increasing, with greater than 200 publications on Medline as of January 2005. There is no doubt that the test is superior to the BT in the detection of VWD and a number of platelet defects and therefore can provide a potentially useful screening tool for the diagnosis and work up of both paediatric and adult haemostatic disorders. Table I summarizes the potential utilities of the PFA-100 in clinical practice and highlights the advantages and disadvantages of the test. The test however, is not diagnostic and although abnormal CTs are an indication of platelet dysfunction, they are non-specific to any disorder, without knowledge of other variables that influence the test, e.g. VWF, full blood count and other platelet function tests. Although early comparisons with the BT were favourable, more recent evidence suggests that screening tests, such as the BT and PFA-100®, have limited value in the diagnosis of patients presenting with mucocutaneous bleeding. This is because the PFA-100® appears to have equivalent low sensitivity compared with the BT in the detection of PSDs and SPD, conditions which are often frequently encountered. Clinicians should always perform a full range of platelet function tests where clinical suspicion is strong and where exclusion of a platelet defect is essential, even if the PFA-100® CADP and CEPI CTs are normal. However, the test does offer a high negative predictive value for excluding VWD and rare forms of severe platelet defects (e.g. Glanzmann’s Thrombasthenia and Bernard Soulier syndrome). The PFA-100® may also be useful as a preoperative screening tool to identify and manage patients with impaired primary haemostasis. The test appears particularly useful for monitoring responses to DDAVP therapy. The PFA-100®, although of limited value as a screening tool, can still offer clinicians and laboratories the comfort of a rapid test result well before other laboratory results become available. Although further studies are required to help define the exact utilities of the PFA-100®, the test does represent a significant advance over the BT and provides a rapid, simple and reliable measure of platelet function.

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**References**


