Uniquely Simulates the \textit{in vivo} function of Platelets in Primary Hemostasis

"The PFA-100\textsuperscript{®} device provides an attractive test not only for the specialized haemostasis laboratory, but also to small, non-specialized haematology laboratories, pharmaceutical research and development groups, and cardiology, paediatric and other departments interested in platelet function...the PFA-100\textsuperscript{®} device is an attractive, simple and reliable means of assessing platelet function rapidly without the operators requiring specialized knowledge or training."

P. Harrison, M.S.C. Robinson, I.J. Mackie, et al. \\
\textit{Blood Coagulation and Fibrinolysis}. 1999.\textsuperscript{1}

\textbf{Simulation Starts with High Shear Flow}

Based on work by Kratzer and Born,\textsuperscript{2,3} the PFA-100\textsuperscript{®} \textit{In Vitro} Diagnostic System incorporates a high shear flow system to simulate the \textit{in vivo} hemodynamic conditions of platelet adhesion and aggregation as encountered at a vascular lesion. The system aids in the rapid detection of platelet dysfunction in primary hemostasis.
“Typically, the PFA-100® test takes less than 5 minutes to run... The potential cost savings for an institution with a large volume of tests are, therefore, considerable.”

J. Francis, D. Francis, L. Larson, et al. 

**Generates Objective, Accurate and Reproducible Results**

The self-contained, disposable cartridges include all functional elements required for testing, assuring consistency within each lot and limiting test variability. Two types of cartridges are available.

**Closure Time Reference Range**

<table>
<thead>
<tr>
<th>Cartridge</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>COL/EPI</td>
<td>94–193 seconds</td>
</tr>
<tr>
<td>COL/ADP</td>
<td>71–118 seconds</td>
</tr>
</tbody>
</table>

Results are reported as Closure Time. Closure Time is dependent on platelet count and is sensitive to hematocrit.

The Collagen/Epinephrine Cartridge is used to detect platelet dysfunction induced by intrinsic platelet defects, von Willebrand factor, functional deficiencies or exposure to platelet inhibiting agents.

The Collagen/ADP Cartridge is used for subsequent testing to determine if an abnormal result with the Collagen/Epinephrine Cartridge was caused by the effect of acetylsalicylic acid (ASA) or medications containing ASA.
Clinical Performance of the PFA-100® in Detecting von Willebrand disease

Delivers the Safety of No Sample Preparation

- No special sample collection requirements; small sample volume required (800 µL)
- All biological material remains in the test cartridge, minimizing operator/blood contact for improved safety and consistency, avoiding instrument contamination and facilitating biohazard disposal
- Patient not needed to be present; samples are stable for up to 4 hours

Saving Time and Money

The fully automated PFA-100® provides results in five minutes†, minimizes technician time and operator interface, and may be less costly than traditional methods.‡

Perfect for All Skill Levels

Easy to use, investigators have described the PFA-100® System as an attractive, simple and reliable means of assessing platelet function rapidly, without requiring specialized knowledge or training.§

* Specimens collected in 3.8% (0.129 M) buffered sodium citrate, from 176 ostensibly healthy individuals were evaluated to establish a reference range. Each laboratory should determine their own Closure Time reference ranges.
† Two patients with Type 2N were omitted from the evaluation.
‡ Includes 3.0 minute sample incubation.
The adhesion of platelets to collagen and von Willebrand factor is generally believed to induce the secretion of substances such as ADP and serotonin and the expression of binding sites on platelet glycoprotein (GP) IIb/IIIa.

Platelets under shear stress come in contact with exposed subendothelial collagen and vWF of the damaged vessel wall.

This secretion, by adhering platelets, induces more platelets to be recruited and activated at the site of the lesion.

Aggregating at the site of the damage, the platelets form a hemostatic plug, arresting the bleeding.
The PFA-100® Analyzer has been demonstrated to accurately assess vWF-dependent platelet function and detect other platelet defects in adults and children under high shear stress in complex patient populations, such as those seen in tertiary care centers.

“Concurrent illnesses do not appear to adversely influence the ability of the PFA-100® to detect shear-induced abnormalities in von Willebrand factor and/or platelets.”


Identify Inherited or Acquired Platelet Disorders

The PFA-100® System aids in the detection of platelet dysfunction related to the most common congenital bleeding disorder, von Willebrand disease. Mild cases of vWD can be particularly challenging because it is not uncommon to have lab values within the normal range. The PFA-100® is of tremendous benefit for detecting patients with vWD, even those with the most common Type 1 disease. The system is sensitive to quantitative and qualitative abnormalities of vWF in plasma, as well as in platelets.

The PFA-100® also detects platelet dysfunction related to other diseases such as Glanzmann’s thrombasthenia.

Evaluate the Cause of Menorrhagia

Menorrhagia affects up to 20% of reproductive-aged women. Studies show a prevalence of vWD in up to 20% of these women and menorrhagia is often the most common initial and presenting symptom in patients with Type 1 vWD. Because this problem is often considered to be a gynecologic rather than a hematologic problem, misdiagnosis can result in unnecessary procedures such as dilation and curettage, blood transfusions and/or hysterectomy. In fact, some studies indicate that about 5% of hysterectomies are performed because of excessive bleeding that may be caused by vWD. Moreover, about 20% of hysterectomies involve uteri that demonstrate no histologic abnormality.
Assess Drug-Induced Platelet Dysfunction

Some patients may be unaware they are actually taking aspirin, and both low and high dose aspirin have been shown to increase bleeding time.\textsuperscript{19}

Aspirin is one of the established therapeutic strategies in cardiovascular medicine. However, there is considerable variability between subjects in the sensitivity to the compound.\textsuperscript{20} With a constant dose of aspirin, the antiplatelet effect may vary in an individual over time.\textsuperscript{21} The PFA-100\textsuperscript{®} System may be helpful in assessing a patient’s compliance with aspirin and its antiplatelet effect during therapy.\textsuperscript{20}

The PFA-100\textsuperscript{®} may also be helpful in evaluating the effects of other antiplatelet drugs\textsuperscript{12} and may be useful for rapidly detecting platelet dysfunction in patients being prepared for cardiac catheterization and for those in acute care settings.

Determine Platelet Functionality in High-Risk Pregnancy

The ability to arrest bleeding from a small blood vessel puncture, as may occur during epidural insertion, is mainly a function of primary hemostasis.\textsuperscript{22} The PFA-100\textsuperscript{®} may prove to be a useful tool in the rapid assessment of platelet dysfunction before regional blockade is attempted in patients with disorders such as preeclampsia or gestational thrombocytopenia.\textsuperscript{21}

“The PFA-100\textsuperscript{®} is well adapted to routine testing, as it has the advantage of simplicity and ease of execution. It provides fast results and uses the same citrated blood that is routinely drawn for other coagulation testing; the latter is particularly useful in emergency situations, especially before surgery.”

Blood. 1998.\textsuperscript{10}
Evaluate Platelet Function Preoperatively

Preoperative evaluation of platelet function is of critical importance because every surgical procedure impacts the hemostatic defenses of the patient. Several "screening tests" demonstrate normal results in a number of mild bleeding disorders.

- Postoperative bleeding has been shown to be the most common initial symptom (33%) among males with Type 1 vWD.
- Excessive bleeding is a common complication of cardiac surgery. Up to 3% of patients undergo re-exploration to control postoperative hemorrhage.

With the PFA-100® System, most patients with prolonged Collagen/ADP Closure Times manifest abnormalities in primary hemostasis that could place them at risk during surgery. Further, the PFA-100® may assist in identifying patients who have a substantial postoperative bleeding risk due to a platelet dysfunction.

It is reasonable to assume that a means of assessing platelet function in "real time" may, in the future, allow more appropriate direction of transfusion therapy, which may reduce unnecessary transfusions. The negative consequences associated with allogeneic transfusions have significant health implications, such as the risk of viral and bacterial contamination, endotoxic shock, circulatory overload and immunomodulation. As important as the morbidity and mortality issues, transfusions have been correlated with significantly greater lengths of stay, as well as increased resource consumption and hospital charges.

Augment Other Hemostasis Tests

The PFA-100® System provides rapid, quantitative, clinically relevant evaluations of platelet function, augmenting subjective, imprecise and clinically impractical methods that provide insufficient information.

- Prothrombin Time and Activated Partial Thromboplastin Time only assess the second phase of hemostasis, i.e., the patients' extrinsic and intrinsic clotting ability.
- Platelet Count only provides a number and not the functional ability of platelets.
- Aggregometry is expensive, labor intensive and requires highly specialized technicians to perform and interpret test results.

"The failure to avoid post operative bleeding and related complications in patients with vWD...constitutes a major public health problem."

Ohad Ziv and M.V. Ragni.

References:


Photo Captions:

On the cover: Photomicrograph of two megakaryocytes forming platelets from their cytoplasmatic extensions.

Inside cover: Scanning electron micrograph of human red blood cells, monocyte (orange), T lymphocyte (green), and activated platelets (blue).

On page 3 and inside back cover: Scanning electron micrograph of platelets from their cytoplasmatic extensions.

Inside back cover: Scanning electron micrograph of human red blood cells, monocyte (purple), activated platelets (blue) against a background of serum proteins.
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