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REVIEW

Platelet function analysis

Paul Harrison*

Oxford Haemophilia Centre & Thrombosis Unit, Churchill Hospital, Oxford OX3 7LJ, UK

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Summary Since the last guidelines for BCSH platelet function testing were written in the late 1980s, many new tests have become available. Previously most platelet function tests were traditionally utilized to aid in the diagnosis and management of patients with platelet and haemostatic disorders. Most traditional tests were also largely restricted to the specialized laboratory or centre. However, nowadays there is also much renewed interest in monitoring the efficacy of anti-platelet therapy and measuring platelet hyper-function. A number of dedicated platelet function instruments have now become available that are much simpler to use and are beginning to be utilized as point of care instruments. These can now provide measurement of platelet function within whole blood without the requirement of sample processing. Some are also beginning to be incorporated into routine clinical use and can be utilized as not only as general screening tests of platelet function but to monitor anti-platelet therapy and to potentially assess both risk of bleeding and/or thrombosis. Modern flow cytometric-based platelet function analysis now also provides a wide variety of specific tests that can assess different aspects of platelet biology that are useful for diagnostic purposes. This review will highlight some of these of new tests/instruments and discuss their potential utility both within the haemostasis laboratory but also as potential point of care instruments.

Introduction

Human platelets are small and discoid in shape, with dimensions of approximately 2.0–4.0 by 0.5 μm, and a mean volume of 7–11 fl.[1] They are the second most numerous corpuscle in the blood normally circulating at between 150–450 $\times 10^9$/l. Platelets are anucleated cells derived from megakaryocytes and typically circulate for 10 days.[1] Their shape and small size enables the platelets to be pushed to the edge of vessels, placing them in the optimum location required to constantly survey the integrity of the vasculature. Platelets are also surprisingly multifunctional and are involved in many pathophysiological processes including haemostasis and thrombosis, clot retraction, vessel constriction and repair, inflammation including promotion of atherosclerosis, host defence and even tumour growth/metastasis (Fig. 1). Although, any test(s) of platelets could therefore potentially measure any one or more of these vital processes, the majority of available tests focus only on those function(s) involved directly in haemostasis.

Upon vessel wall damage, platelets undergo a highly regulated set of functional responses including adhesion, spreading, release reactions, aggregation, exposure of a procoagulant surface, microparticle formation and clot retraction (Fig. 2). All of these platelet responses function to rapidly form a haemostatic plug that occludes the site of damage to prevent blood loss.[2,3] When there

* Tel.: +44-1865-225305; fax: +44-1865-225299.
E-mail address: paul.harrison@ndm.ox.ac.uk.

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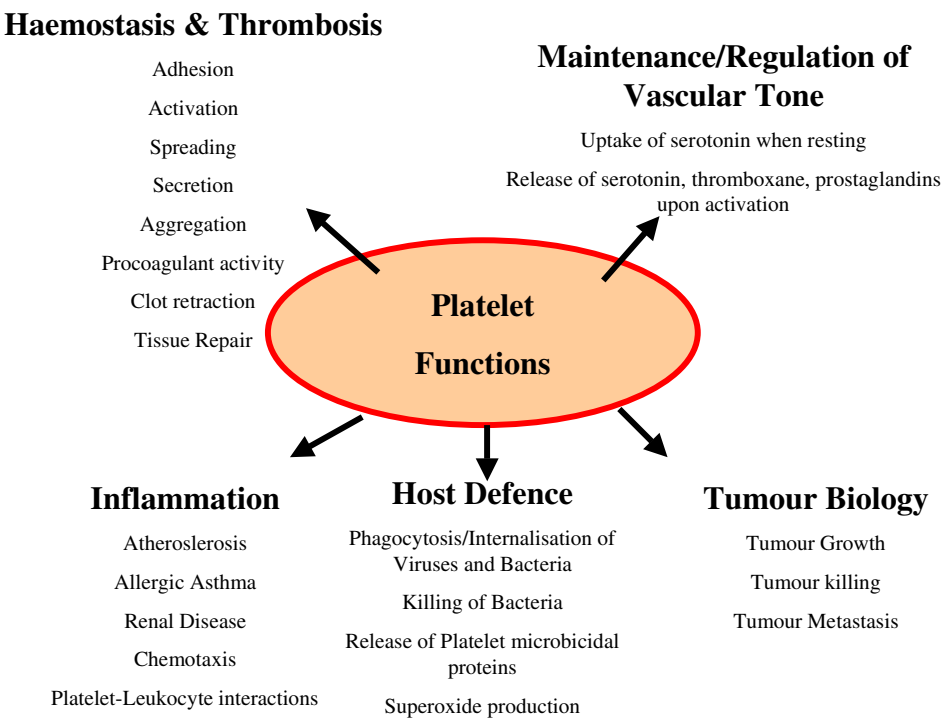

Figure 1 The multifunctional platelet. Platelets are involved in many pathophysiological processes, in addition to haemostasis and thrombosis, namely maintenance of vascular tone, inflammation, host defence and tumour biology.

is a defect in any of these functions and/or platelet number, haemostasis is usually impaired and there may be an associated increased risk of bleeding. In contrast, a marked increase in platelet number or reactivity can lead to inappropriate thrombus formation. Arterial thrombi can also develop within atherosclerotic lesions resulting in stroke and myocardial infarction, two of the major causes of morbidity and mortality in the western world.[4] Anti-platelet therapy can therefore be beneficial in the treatment and prophylaxis of arterial thrombotic conditions, but must be carefully administered without increasing the risk of bleeding to an unacceptable level.[1]

The main use of platelet function tests has been traditionally to identify the potential causes of abnormal bleeding,[5] to monitor pro-haemostatic therapy in patients with a high risk of bleeding and to ensure normal platelet function either prior to or during surgery.[6,7] However, they are increasingly being utilised to monitor the efficacy of anti-platelet therapy and to potentially identify platelet hyperfunction to predict thrombosis.[6,8] For a full list of potential clinical uses of platelet function tests see Table 1.

History of platelet function testing

Platelets were first described by the remarkably early observations of Bizzozero in the late 1800s.[9] Not only did he identify platelets as distinct corpuscles within human blood but he observed them forming thrombi within damaged areas of vessel wall using real-time microscopy. Today, modern imaging methods are utilised to study in detail the same real time interactions of platelets with the vessel wall and dynamics of thrombus formation.[10]

Table 2 illustrates a list of traditional tests of platelet function including the in vivo bleeding time and platelet aggregometry.[11] In contrast to coagulation defects, where screening tests e.g. the activated partial thromboplastin time (APTT) and prothrombin time (PT) are inexpensive and fully automated, platelet function defects are more difficult to diagnose because there are no definitive screening tests. Indeed, no current or future platelet function test is likely to be a 100% sensitive, due to the large number and variety of platelet defects. The current evaluation of a potential platelet defect usually involves platelet aggregation and/or measurement of granule content/release. These tests are labour intensive, costly, time consuming and require a fair degree of expertise and experience to perform and interpret. Also additional expensive specialist tests are often required (e.g. flow cytometry and platelet nucleotides). Since the late 1980s when the last published platelet function testing guidelines were written by the BCSH,[12] a number of newer tests of platelet function have become available, including