

# Diagnostic repertoire for investigation of suspected Platelet Function Disorders

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## INTRODUCTION

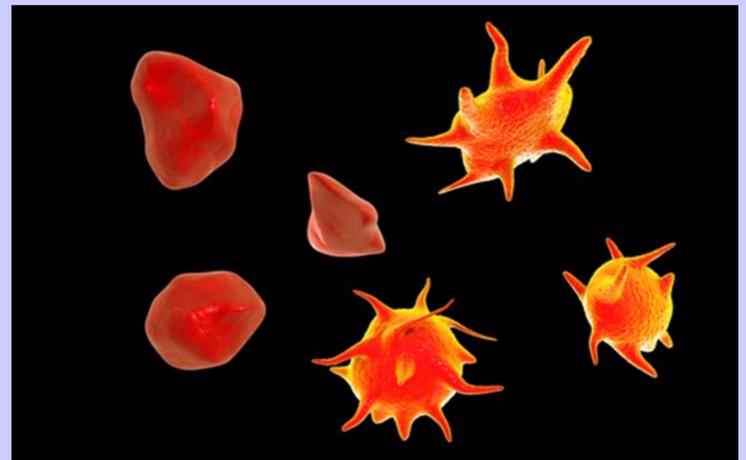
- Patients present with suspected bleeding disorders for investigation and diagnosis throughout life. Severe conditions usually manifest in neonatal or early childhood requiring urgent clinical intervention, whereas with mild disorders referral is often dependent on patient's concern relating to chronic symptoms or unexplained bleeding associated with trauma or surgery or detected as part of other investigations.
- Congenital bleeding disorders are rare but there is a higher frequency associated with clotting factor deficiencies with diagnostics and resources focused in this area of first line investigations.
- Investigation of suspected platelet function disorders is more complex and without an appropriate diagnostic repertoire mild platelet function defects may be under detected.

## METHODS

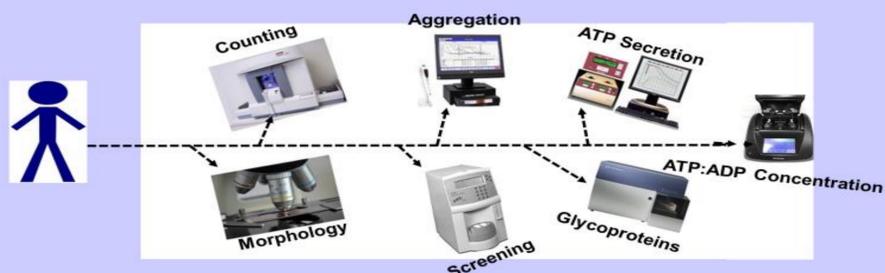
- Data was collected over an 18-month period on patients (N = 118) who had platelet function studies performed for investigation of a suspected congenital or acquired bleeding disorder.
- Patients were advised not to take "over the counter" Non-steroidal Anti-inflammatory drugs for 2 weeks prior to appointment and prescription pain relief was stopped if possible or testing postponed.
- Other potential interfering prescription medication was not stopped to enable identification of possible acquired defect.
- Full blood count (FBC) was performed (Advia 2020 Siemens UK), platelet function screening using collagen-epinephrine (CEPI) and collagen-ADP (CADP) cartridges (PFA-100 Siemens), platelet-rich platelet aggregation with range of agonists (PAP-8 Alpha UK), whole blood maximum ATP secretion with thrombin (Chronolog USA) and platelet ADP and ATP nucleotide concentrations (Luminometry).

## AIM

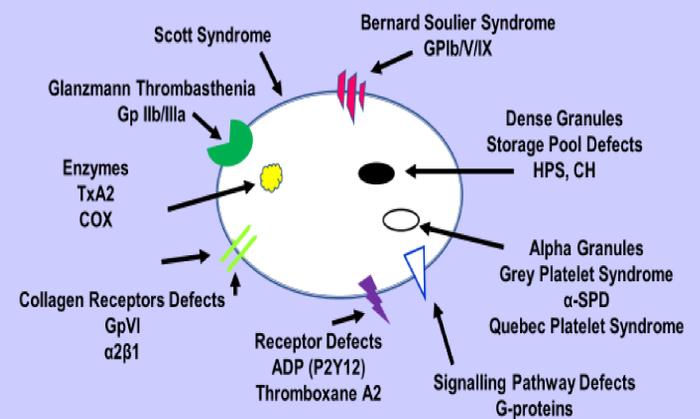
To audit local diagnostic test repertoire to identify detection level of platelet function abnormalities which may be congenital or acquired associated with other underlying pathologies or medication and determine contribution of individual tests methodologies to diagnosis.



## Platelet Function Investigations



## Platelet Function Disorders



## RESULTS

Audit data by method for the total number of patients showed:

- Abnormal platelet function screening with CEPI = 14% and CADP = 19.5%
- Abnormal platelet aggregation = 26%
- Abnormal ATP secretion = 7%
- Abnormal platelet nucleotide concentrations = 18.5%

- In total 56.6% of patients were identified with abnormal platelet function test results, with 44% patients having one abnormal result according to method, 30% two abnormal, 24% three abnormal and 2% five abnormal results (see Tables 1, 2 and 3 below).
- The audit showed majority of abnormalities were associated with Storage Pool "Type" defects characterised with either reduced nucleotide concentration, reduced secretion or receptor defects.

**Table 1: Abnormal Patient Results According to Method**

TEST	% Patients Abnormal	Total Number Abnormal
PFA - CEPI	14	12
PFA - CADP	19.5	16
Platelet Aggregation	26	22
ATP Secretion	7	6
Platelet Nucleotides	18.5	16

**Table 2: Abnormal Result Combinations**

Test Combinations	Number of Abnormal Patients
PFA CEPI + CDP only	1
PFA CEPI only	1
PFA CADP only	3
CEPI + CADP + Aggregation	4
PFA CEPI + Aggregation	4
PFA CADP + Aggregation	4
CEPI + CADP + Nucleotide concentration	6

**Table 3: Abnormal Result Combinations**

Test Combinations	Number of Abnormal Patients
Platelet aggregation only	11
Platelet aggregation + ATP secretion	3
Platelet aggregation + Nucleotide concentrations	6
Aggregation + ATP secretion + Nucleotide conc.	3
ATP secretion + Nucleotide concentrations	1
CEPI + CADP + Aggregation + ATP secretion + Nucleotide concentrations	1

## CONCLUSIONS

- Audit data has shown that current test repertoire detects a significant number of patients (N = 56.6%) with mild congenital or acquired platelet function disorders.
- This level of abnormal result detection is encouraging as in most cases these patients have a strong bleeding history and first line factor deficiency investigations have not identified an underlying diagnostic cause of symptoms.
- However, it has highlighted the requirement for a comprehensive testing panel to provide a range of detection methodologies to provide scope of sensitivity to individual patient platelet abnormalities to enable diagnosis.
- Platelet aggregation alone is insufficient to detect a number of patients with mild congenital or acquired platelet disorders and ATP secretion and nucleotide quantitation increases rate of detection and provides distinction between storage, secretion and receptor defects.
- With the recent establishment of Genetic/Genomic Diagnostic Hubs and increasing identification of pathological mutations, platelet genetic testing in conjunction with abnormal phenotype results will aid in improved diagnosis and classification of mild platelet disorders.