
Platelet Function Measurement

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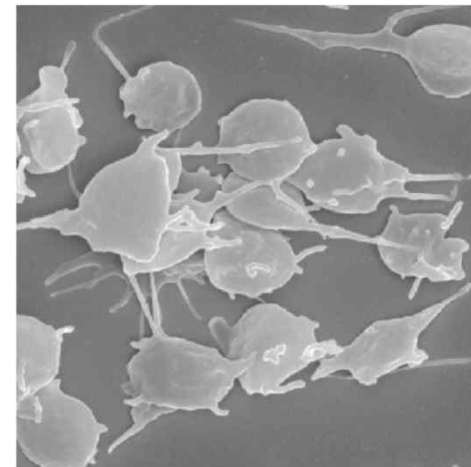
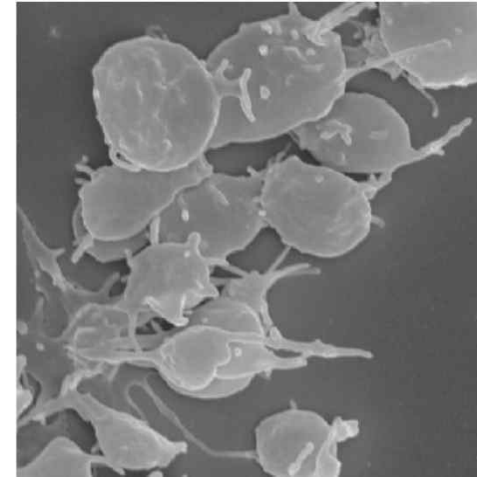
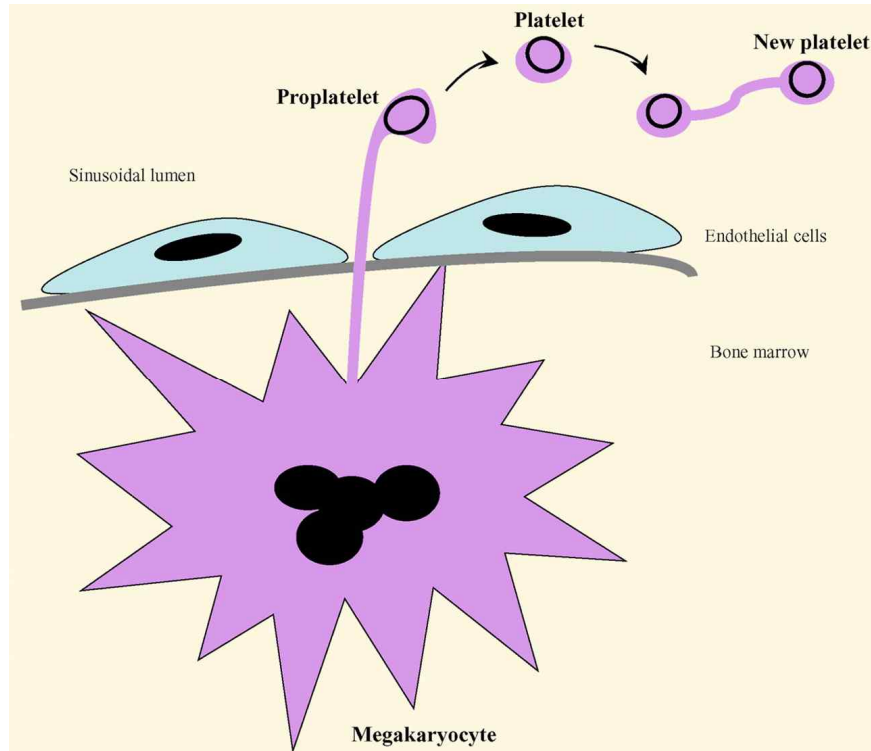
Contents

- Role of Platelets in Hemostasis
 - Various Platelet Function Tests
 - Future Directions
-

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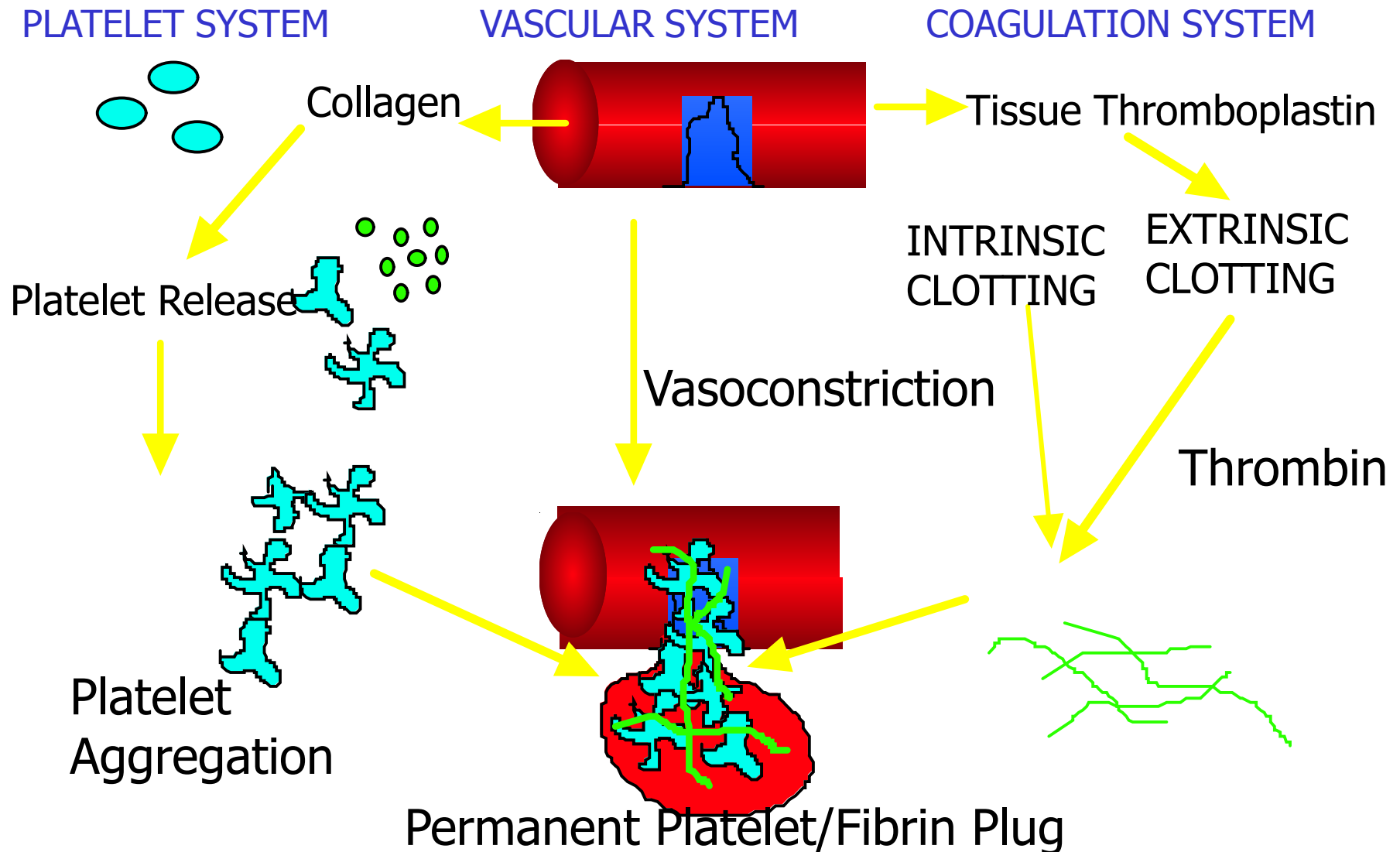
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Platelet Morphology

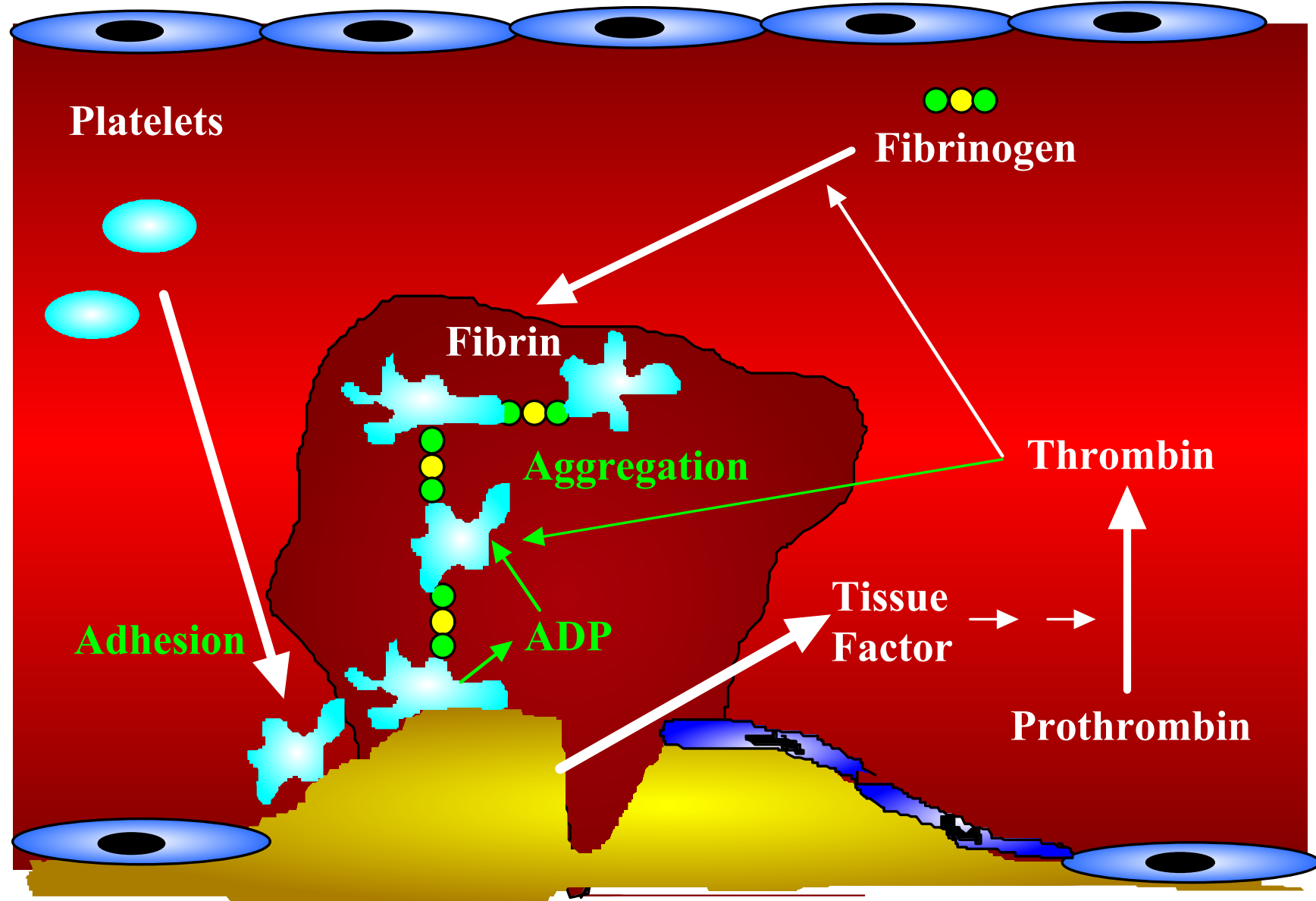


Blood 2010;115:3801-9

Global Scheme of Hemostasis



Primary Hemostasis



Contents

- Role of Platelets in Hemostasis
- **Various Platelet Function Tests**
- Future Directions

Platelet Function Tests

Perspectives

- Important role in diagnosis of many congenital and acquired bleeding disorders
 - Testing of platelet function has not been standardized
 - Challenges to test standardization
 - Heterogeneity in platelet disorders
 - Lack of diagnostic criteria
 - Limited evidences
 - Few guidelines on testing
 - No guidelines on test interpretation
-

Platelet Function Tests



Platelet aggregometry



Flow cytometry



Accumetrics®

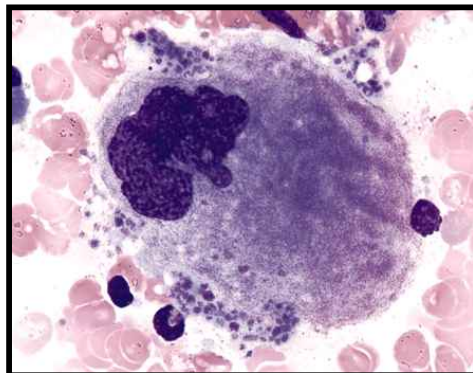
Item	Data	Unit	Item	Data	Unit
WBC	5.88	10 ³ /UL	NEUT#	2.93	10 ³ /UL
RBC	3.81	10 ⁶ /UL	LYMPH#	2.41	10 ³ /UL
HGB	12.2	g/dL	MONO#	0.39	10 ³ /UL
HCT	36.3	%	EO#	0.13	10 ³ /UL
MCV	95.3	fL	BASO#	0.02	10 ³ /UL
MCH	32.0	pg	NEUT%	49.9	%
MCHC	33.6	g/dL	LYMPH%	41.0	%
PLT	210	10 ³ /UL	MONO%	6.6	%
RDW-SO	45.8	fL	EO%	2.2	%
RDW-CV	13.2	%	BASO%	0.3	%
PDW	13.1	fL			
MPV	11.1	fL			
P-LCR	33.1	%			
PCT	0.23	%			
RET%		%			
RET#		10 ⁶ /UL			
IRF		%			
LFR		%			
HFR		%			
HFR		%			
HRBC#		10 ³ /UL			
NRBC%		/100WBC			



Multiplate® analyzer



Thromboelastography



PFA-100®



Impact®

Platelet Function Tests

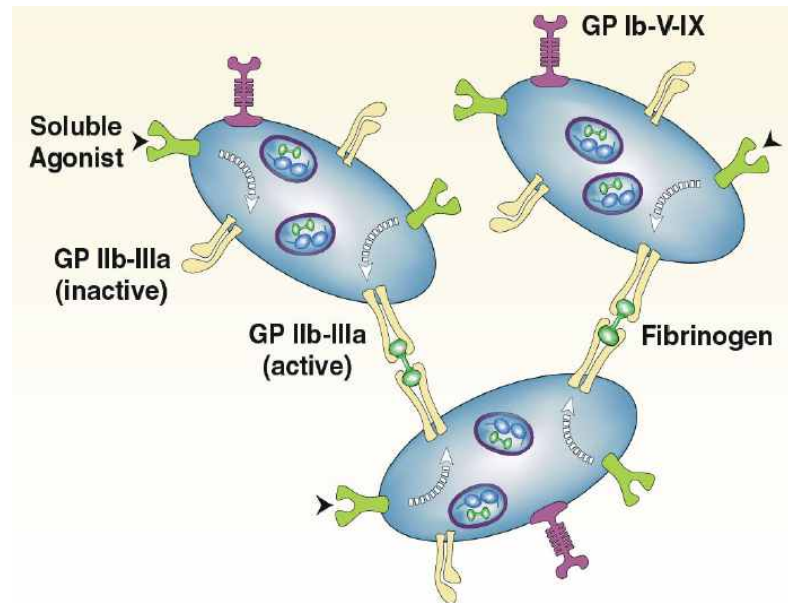
Bleeding Time (BT)



- By Duke (1910) & Ivy (1941)
- In vivo test
- Measure of primary hemostasis
- **Rarely used in developed nations**
- Highly dependent on operator
- Influenced by a variety of variables
- Insensitive to mild disorders
- Now replaced by many alternatives

Platelet Function Tests

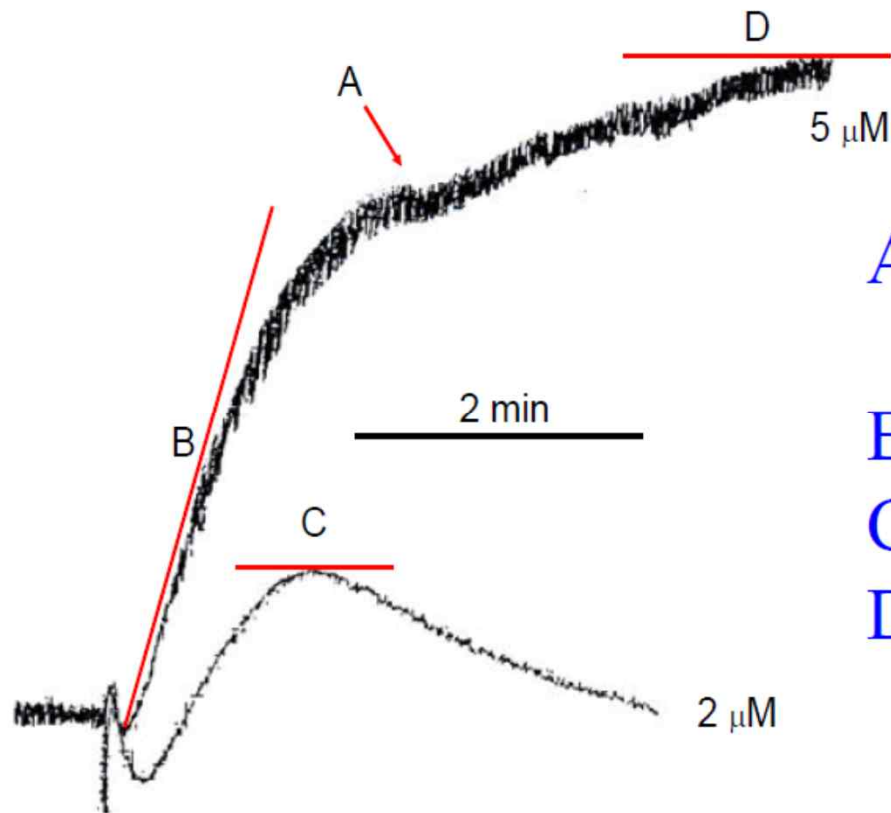
Platelet Aggregometer



Measure light transmission through a test sample containing platelets in suspension that increases when platelets are aggregated by agonists

Platelet Function Tests

Platelet Aggregometer



A. threshold of 2nd wave aggregation

B. initial rate of aggregation

C. % maximum aggregation

D. % final aggregation

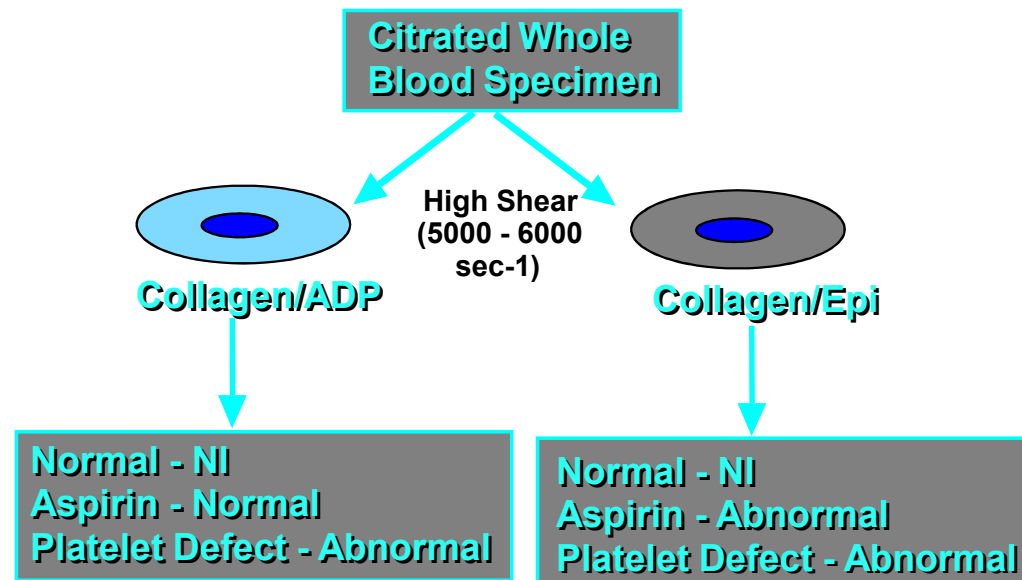
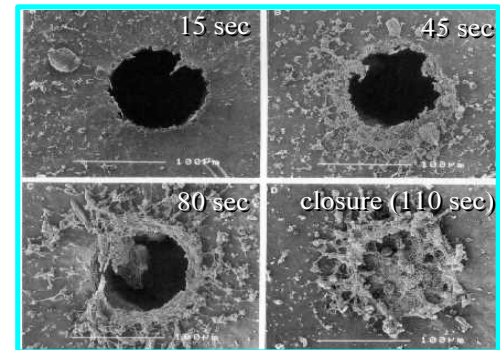
Platelet Function Tests

Platelet Aggregometer

- **Most common test used to assess platelet function**
 - Time consuming, technically challenging
 - Affected by many pre-analytical and analytical variables
 - Proper use of agonists and concentration
 - Diagnosis of several bleeding disorders associated with inherited or acquired platelet dysfunction
 - Monitoring of anti-platelet agents: Not encouraged by ISTH
 - Standardization: CLSI or ISTH guidelines
 - Quality assurance issues: CAP, NASCOLA, UK NEQAS
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Platelet Function Tests

Platelet Function Analyzer (PFA)-100



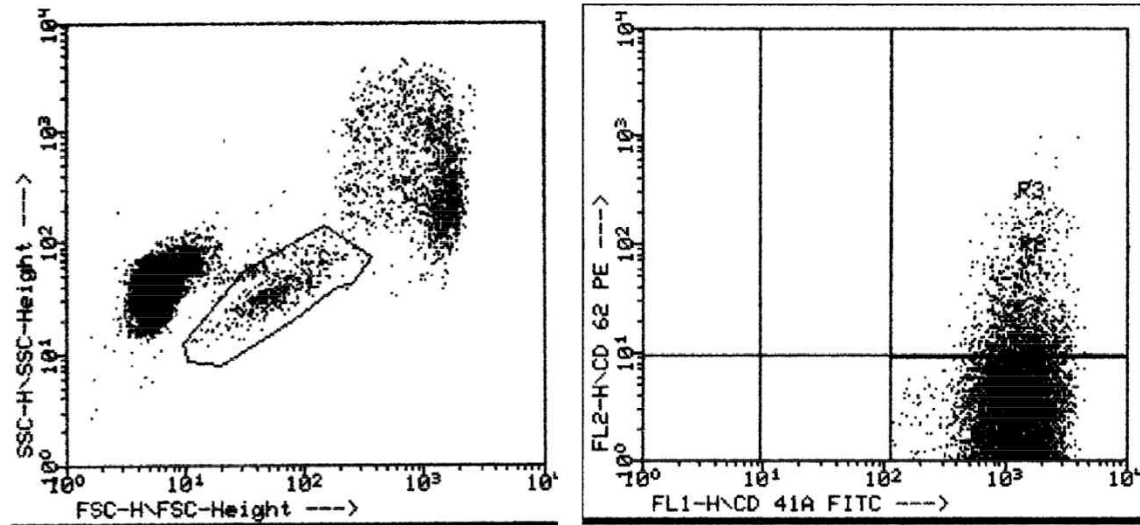
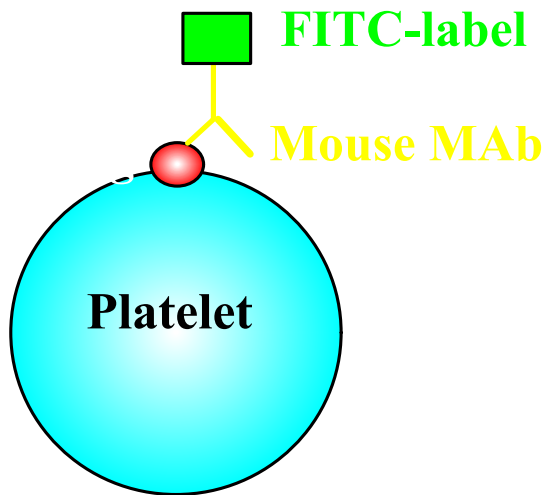
Platelet Function Tests

Platelet Function Analyzer (PFA)-100

- **Most widely used for global primary hemostasis**
 - Very quick and easy to perform, well standardized
 - Small volume of venous blood (0.8 mL)
 - Low platelet count ($<100,000/\mu\text{L}$) or low Hct ($<30\%$) may cause long closure time (CT)
 - Very sensitive, but non-specific screening tool
 - Normal PFA-100 results can help exclude some severe platelet dysfunctions (Glanzmann's, Bernard-Soulier)
 - Role in therapeutic monitoring remains to be established
-

Platelet Function Tests

Flow Cytometer



- Deficiency of surface glycoproteins
- Detection of activated platelets
- Platelet secretion studies

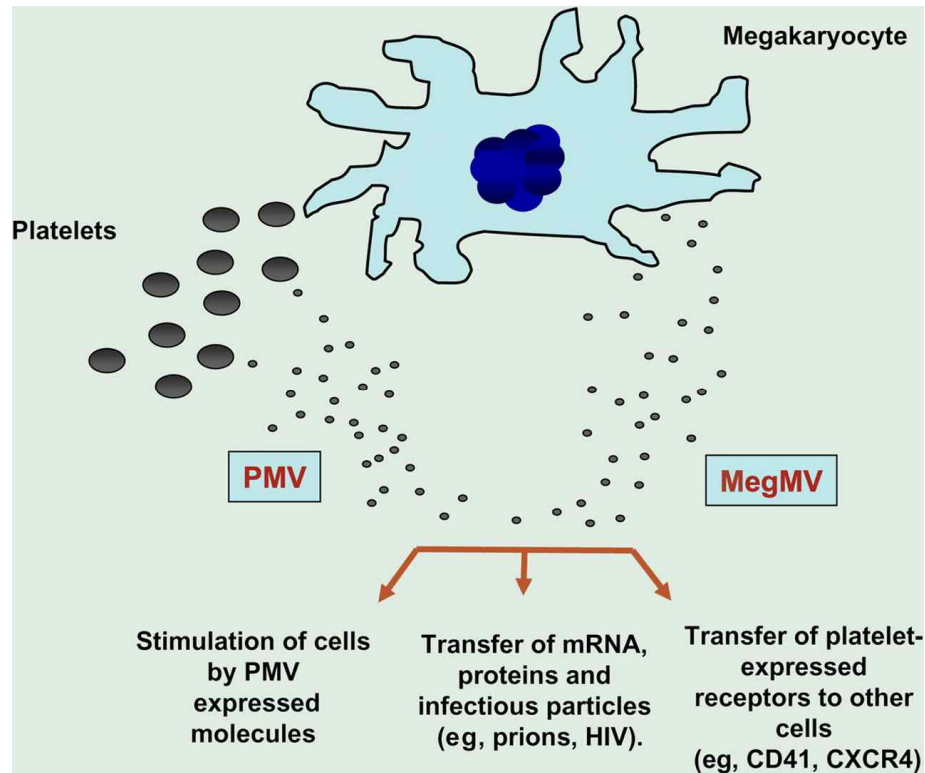
Platelet Function Tests

Flow Cytometer

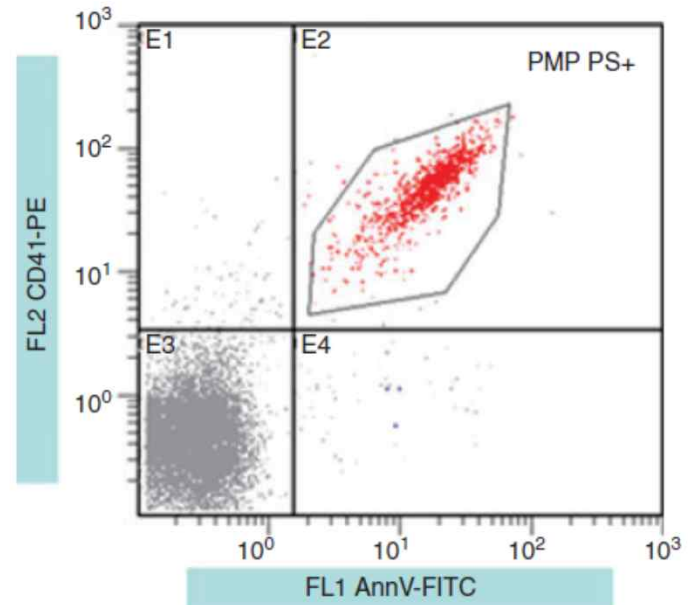
- Diagnosis of Platelet disorders
 - Quantification of receptor density
 - Detection of activated platelets
 - Monitoring platelet responses to agonists
 - Monitoring of platelet apoptosis
 - Monitoring antiplatelet drugs
 - Platelet associated IgG
 - Platelet production in thrombocytopenia
 - Signal transduction: VASP-P
 - Disadvantages: Specialized operator, expensive
-

Platelet Function Tests

Flow Cytometer



Platelet Microparticles



Blood 2009;113:981-2

Platelet Function Tests

Point-of-Care Testing (POCT)

- Definition: Diagnostic test at or near the site of patient
 - PFA-100, Thromboelastography, VerifyNow, Plateletworks
 - Primarily to measure the effect of antiplatelet drugs
 - Utility for screening and diagnosis of platelet function defects: Not been examined systematically
 - Very limited information about pre-test variables
 - Limited QA material available
 - **Identification of patients with aspirin and clopidogrel resistance**
-

Platelet Function Tests

Thromboxane Metabolites

- **Serum TxB₂ and urinary 11-dehydro TxB₂**
 - Amplify the activation response and recruit additional platelets to the site of clotting
 - Determined by immunoassays or mass spectrometry
 - Indirect measure, not entirely platelet-specific
 - Dependent on COX-1 activity
 - Potential effects of renal function
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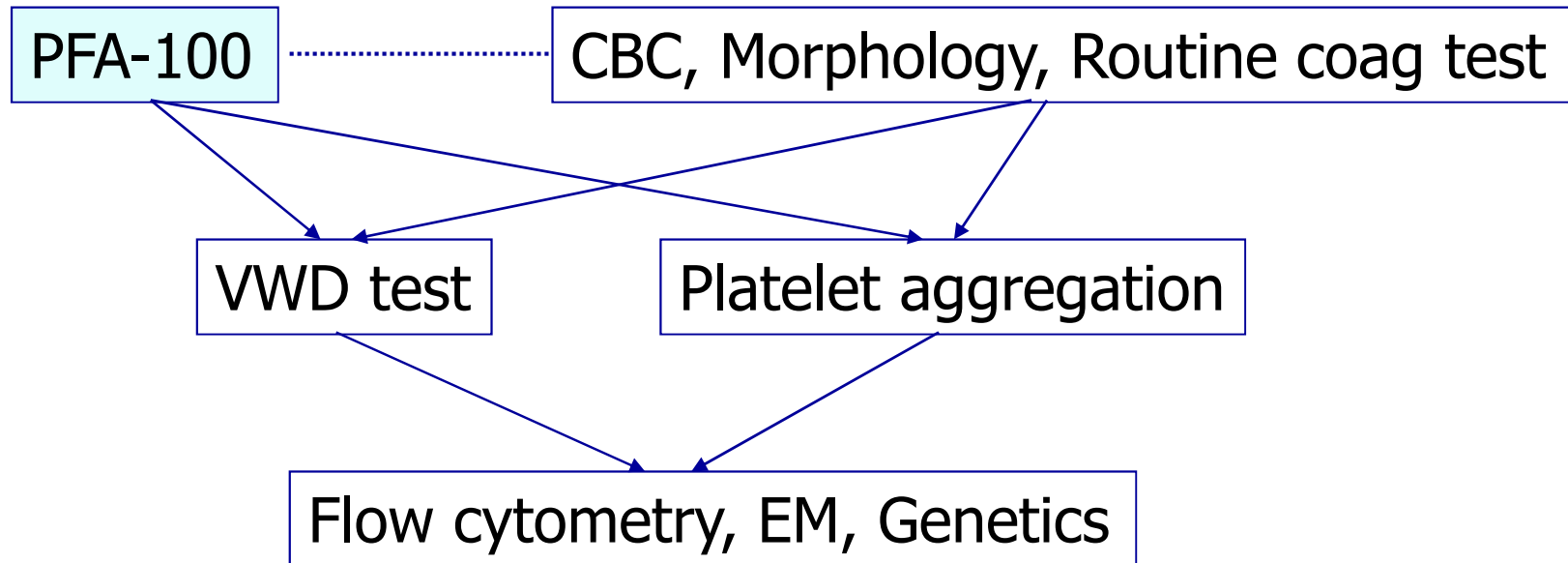
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-

Guidelines on Tests

- ISTH guidelines
 - PFA-100 closure time in the evaluation of platelet disorders and platelet function, *J Thromb Haemost 2006*
 - Aspirin resistance: position paper of the Working Group on Aspirin Resistance, *J Thromb Haemost 2005*
 - Result of a Worldwide Survey on the Assessment of Platelet Function by Light Transmission Aggregometry, *J Thromb Haemost, in press*
 - CLSI guidelines
 - Platelet Function Testing by Aggregometry, *CLSI 2008*
-

Algorithm for Tests



Summarized from Clin Chem Lab Med 2010;48:579-98

Summary

- Platelet function tests
 - Traditionally used to diagnose platelet dysfunction
 - Newer tests to supplement bleeding time and platelet aggregation: PFA-100, flow cytometer, VerifyNow, etc.
 - Quality assurance issues
 - New role for platelet function testing
 - Monitoring the effects of antiplatelet drugs
 - Future challenges
 - Molecular basis of platelet biology
 - Platelet genomics and proteomics
 - Platelet transcriptomics
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Welcome to Busan

