PLATELETS IN HEMATOLOGIC AND CARDIOVASCULAR DISORDERS

A Clinical Handbook

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PREFACE

Progress in the field of platelet research has accelerated greatly over the last few years. If we just consider the time elapsed since our previous book on platelets (*Platelets in Thrombotic And Non-Thrombotic Disorders,* 2002), over 10 000 publications can be found in a PubMed search using the keyword "platelets."

Many factors account for this rapidly expanding interest in platelets, among them an explosive increase in the knowledge of the basic biology of platelets and of their participation in numerous clinical disorders as well as the increasing success of established platelet-modifying therapies in several clinical settings. All of this has led to the publication of several books devoted to platelets in recent years. Nevertheless, it is surprising that none of these is a handbook that presents a comprehensive and pragmatic approach to the clinical aspects of platelet involvement in hematologic, cardiovascular, and inflammatory disorders and the many new developments and controversial aspects of platelet pharmacology and therapeutics.

Based on these considerations, this new book was not prepared simply as an update of the previous edition but has undergone a number of conceptual and organizational changes.

A new editor with a specific expertise in hematology, Dr. José López, has joined the group of the editors, bringing in a hematologically oriented view. The book has been shortened and is now focused on the clinical aspects of the involvement of platelets in hematologic and cardiovascular disorders. Practical aspects of the various topics have been strongly emphasized, with the aim of providing a practical handbook useful for residents in hematology and cardiology, medical and graduate students, physicians, and also scientists interested in the broad clinical implications of platelet research. We expect that this book will also be of interest to vascular medicine specialists, allergologists, rheumatologists, pulmonologists, diabetologists, and oncologists.

The book has been organized into four sections, covering platelet physiology, bleeding disorders, thrombotic disorders, and antithrombotic therapy. A total of 26 chapters cover all the conventional and less conventional aspects of platelet involvement in disease; emphasis has been given to the recent developments in each field, but always mentioning the key discoveries that have contributed to present knowledge. A section on promising future avenues of research and a clear table with the heading "Take-Home Messages" have been included in each chapter. A group of leading experts in the various fields covered by the book, from eight countries on three continents, have willingly agreed to participate; many of them are clinical opinion leaders on the topics discussed. All chapters have undergone extensive editing for homogeneity, to help provide a balanced and complete view on the various subjects and reduce overlap to a minimum.

We believe that, thanks to the efforts and continued commitment of all the people involved, the result is a novel, light, and quick-reading handbook providing an easy-to-consult guide to the diagnosis and treatment of disorders in which platelets play a prominent role.

Additional illustrative material is available online through the site of Cambridge University Press (www.cambridge.org/9780521881159).

This book would have not been possible without the help of our editorial assistants (M. Sensi, R. Stevens) and of several coworkers in the Institutions of the individual editors (S. Momi, E. Falcinelli). An excellent

collaboration with the team at Cambridge University Press (Daniel Dunlavey, Deborah Russell, Rachael Lazenby, Katie James, Jane Williams, and Eleanor Umali) has also been crucial to the successful accomplishment of what has seemed, at certain moments, a desperate task.

We hope that this book will be interesting and useful to readers as much as it has been for us.

The Editors

GLOSSARY

$\alpha_{IIb}\beta_3$	$\alpha_{IIb}\beta_3$ or glycoprotein IIb-IIIa
$\alpha_{IIb}\beta_3$, $\alpha_2\beta_1$	Platelet integrins
$\alpha_M\beta_2$, $\alpha_L\beta_2$	Leukocyte $\beta 2$ integrins
$\alpha_v\beta_3$	Vitronectin receptor
β-TG	β-thromboglobulin
AA	Arachidonic acid
ACD	Citric acid, sodium citrate, dextrose
ACS	Acute coronary syndrome
ADP	Adenosine-5'-diphosphate
AKT	Serine/threonine protein kinase
APS	Antiphospholipid antibody syndrome
ASA	Acetylsalicylic acid
ATP	Adenosine-5'-triphosphate
AVWS	Acquired von Willebrand syndrome
BSS	Bernard–Soulier syndrome
BT	Bleeding time
CAD	Coronary artery disease
cAMP	Cyclic AMP
CAMT	Congenital amegacaryocytic thrombocytopenia
CD40L (CD154)	CD40 ligand
CD62P	P-selectin
CFU	Colony forming unit
cGMP	Cyclic GMP
CHS	Chediak–Higashi syndrome
CML	Chronic myeloid leukemia
COX-1	Cyclooxygenase-1
COX-2	Cyclooxygenase-2
CPD	Citrate-phosphate-dextrose
CRP	C-reactive protein
CVID	Common variable immunodeficiency
DDAVP	L-deamino-8-O-darginine vasopressin
DIC	Disseminated intravascular coagulation
DTS	Dense tubular system
DVT	Deep venous thrombosis
EC	Endothelial cells
ECM	Extracellular matrix
EDHF	Endothelium-derived hyperpolarizing factor
EDTA	Ethylene diamine tetracetic acid
EGF	Epidermal growth factor
eNOS	Endothelial nitric oxide synthase
EP	PGE_2 receptor
EPCs	Endothelial progenitor cells
ERK	Extracellular signal-regulated kinase
ET	Essential thrombocytemia
FAK	Focal adhesion kinase
Fbg	Fibrinogen
Fn	Fibrin
GEF	Guanine nucleotide exchange factor
GP	Glycoprotein (e.g., GP Ib, GP Ib/IX/V)
GPIb	Glycoprotein Ib
GPCR	G protein-coupled receptor
GPS	Gray platelet syndrome
GT	Glanzmann's thrombasthenia
12-HETE	12-(S)-hydroxyeicosatetraenoic acid
HDL	High-density lipoprotein
HIT	Heparin-induced thrombocytopenia
HLA	Human leukocyte antigen
HPA	Human platelet antigen

Glossary

HPS	Hermansky–Pudlak syndrome
5-HT	5-hydroxytryptamine
HUS	Hemolytic uremic syndrome
ICAM-1	Intercellular adhesion molecule-1
ICAM-2	Intercellular adhesion molecule-2
ICH	Intracranial hemorrhage
IFN	interferon
IL	Interleukin
iNOS	Inducible nitric oxide synthase
IP	Prostacyclin receptor
ITP	Idiopathic thrombocytopenic purpura
IVIG	Intravenous immunoglobulin
JAK	Janus family kinase
JAM	Junctional adhesion molecule
JNK	c-Jun N-terminal kinase
LDL	Low-density lipoprotein
LDH	lactate dehydrogenase
LFA-1	Leukocyte function-associated molecule-1
LMWHs	Low-molecular-weight heparins
LOX-1	Lectin-like oxLDL-1
LPS	Lipopolysaccharide
LT	Leukotriene
MAC-1 (CD11b/CD18)	Leukocyte integrin $\alpha_M\beta_2$
MAIPA	Monoclonal antibody-specific immobilization of platelet antigens
MAPK	Mitogen-activated protein kinase
MAPKKK, MEKK	MAPK kinase kinase
MCP-1	Monocyte chemoattractant protein-1
MDS	Myelodysplastic syndrome
MEK, MAPKK	MAPK/ERK kinase
MF	Myelofibrosis
MI	Myocardial infarction
MIP-1α	Macrophage inflammatory protein-1α
MK	Megakaryocyte
MMPs	Matrix metalloproteinases
MPD	Myeloproliferative disorders
MPV	Mean platelet volume
NAIT	Neonatal allo-immune thrombocytopenia
NFkB	Nuclear factor kB
nNOS	Neuronal nitric oxide synthase
NO	Nitric oxide
NSAID	Nonsteroidal anti-inflammatory drug
NSTEMI	Non-ST–elevation myocardial infarction
OCS	Open canalicular system
PAF	Platelet activating factor
PAIgG	Platelet-associated IgG
PAR	Protease-activated receptor (e.g., PAR1, PAR4)
PDE inhibitors	phosphodiesterase inhibitors
PDGF	Platelet-derived growth factor
PE	Pulmonary embolism
PFA-100®	Platelet Function Analyzer-100®
PG	Prostaglandin
PGH2	Prostaglandin H2
PGI_2	Prostacyclin (prostaglandin I_2)
PI	Phosphatidylinositol
PIP2	Phosphoinositide 4,5 bisphosphate
PIP3	Phosphoinositide 3, 4, 5 tris phosphate
PI3K	Phosphoinositol-3 kinase
PKA	Protein kinase A
PKC	Protein kinase C
PLA_2	Phospholipase A_2
PLTs	Platelets
PMN	Polymorphonuclear cells
PMP	Platelet microparticles
PNH	Paroxysmal nocturnal hemoglobinuria
PPP	Platelet-poor plasma
PR	Platelet reactivity index
PRP	Plateletrich plasma
PS	phosphatidyl serine
PSGL-1	P-selectin glycoprotein ligand-1
PT	Prothrombin time
PTP	Posttransfusion purpura
PTT	Partial thromboplastin time
PUBS	Periumbilical blood sampling
PV	Polycytemia vera

RANTES	Regulated on activation normal T cell-expressed and secreted
RGD	Arg-Gly-Asp
ROS	Reactive oxygen species
SDF-1	Stromal cell-derived factor 1
STEMI	ST-segment-elevation myocardial infarction
TAR	Congenital thrombocytopenia with absent radius
TARC	Thymus and activation-regulated chemokine
TF	Tissue factor
TGF	Transforming growth factor
TMA	Thrombotic microangiopathy
TNF	Tumor necrosis factor
TNFα	Tumor necrosis factor α
TP	Thromboxane A2 receptor
TPO	Thrombopoietin
TTP	Thrombotic thrombocytopenic purpura
TxA_2	Thromboxane A_2
UFH	Unfractionated heparin
UVA, UVB	Ultraviolet A, ultraviolet B
VCAM-1	Vascular cell adhesion molecule-1
VWF	von Willebrand factor
WAS	Wiskott–Aldrich syndrome
WBCs	White blood cells
WP	Washed platelet