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## Preface

We are pleased to present this compilation of methods, protocols, and reviews related to the field of Hemostasis and Thrombosis. This compilation has developed as a work in progress that grew from more humble beginnings. The field of hemostasis and thrombosis is dynamic and ever-developing. Nevertheless, there was a desire to develop a book that provided the current state of the art for methods and protocols used in leading hemostasis and thrombosis laboratories for diagnosis or exclusion of hemorrhagic or thrombotic disease. The initial idea for some 20 chapters was soon recognized to represent an insufficient compilation, and instead developed into the current, more comprehensive textbook.

Indeed, the compilation eventually grew to contain a total of 40 chapters, comprising 31 method/protocol chapters and 9 review/guidance chapters. Contributions have been provided from Australia, North and South America, and many European countries. The compilation is separated into distinct sections.

An initial introductory section provides three overview chapters on: (1) hemostasis and thrombosis, and the contribution of laboratory testing to diagnosis and management of associated disorders; (2) preanalytical issues in hemostasis and thrombosis testing; and (3) the interface between immunotransfusion and hemostasis and thrombosis testing. These chapters provide a comprehensive background to hemostasis and thrombosis testing, pre-analytical issues, and the often under-recognized link of hemostasis and thrombosis testing to immunotransfusion services.

The next section deals with routine coagulation tests, including prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), D-dimer, fibrinogen, thrombin time (TT), and mixing tests. Among other considerations, these chapters provide valuable guidance on (1) how to optimize the verification of mean normal PT (MNPT) and international sensitivity index (ISI) for accurate conversion of PT to INR; (2) how to determine APTT reagent sensitivity to factor deficiencies, heparin, and lupus anticoagulants (LA); (3) how to perform and interpret mixing tests (e.g., PT, APTT); and (4) how to perform and interpret other routine coagulation tests (D-dimer, fibrinogen, TT).

The next section comprises “Thrombophilia” (meaning an increased propensity for thrombosis) related chapters. The section begins with an overview of thrombophilia and associated laboratory testing, and then subsequent chapters reflect methods/protocols for (1) activated protein C resistance (APCR), protein C (PC), protein S (PS), and antithrombin (AT); (2) LA testing by means of dilute Russell Viper Venom Time (dRVVT), APTT, and silica clotting time (SCT); (3) anticardiolipin antibodies and anti- $\beta$ 2 glycoprotein I antibodies; (4) measurement of direct oral anticoagulants (DOACs) such as apixaban, dabigatran, and rivaroxaban; and (5) laboratory testing for heparin-induced thrombocytopenia (HIT).

The succeeding section comprises chapters related to “Bleeding disorders.” There are comprehensive methods/protocols for (1) factor assays by one-stage and chromogenic methods; (2) assessment of factor XIII; (3) detection and measurement of factor inhibitors;

(4) platelet function analysis by light transmission aggregometry (LTA), whole blood aggregometry (WBA), and by flow cytometry; (5) testing for von Willebrand factor antigen and various activities (collagen binding, ristocetin cofactor, glycoprotein Ib binding, factor VIII binding), as well as multimer analysis; and (6) ristocetin-induced platelet aggregation (RIPA), including performance of RIPA mixing studies. This section of the book also includes separate overview/guidance chapters related to (1) diagnosis or exclusion of von Willebrand disease (VWD) and (2) platelet function testing (including preanalytical variables, clinical utility, advantages and disadvantages).

The final section of the book comprises global assays of hemostasis, as well as post-analytical issues in hemostasis and thrombosis testing. This section includes methods/protocols for thrombin generation assays (TGA), the overall hemostatic potential (OHP) assay, and thromboelastography (TEG).

Ultimately, we believe this compilation to reflect the most comprehensive compilation in the field, and we expect it to be well received, especially by workers in the field struggling to identify suitable methods/protocols for hemostasis and thrombosis testing, or otherwise seeking expert guidance on such testing. As leading scientists in the field, we and our colleagues are regularly asked for guidance on hemostasis and thrombosis testing, and we feel that this book represents expert guidance at the high end of conceivable support.

We sincerely thank the Series editor, John Walker, for starting us on this journey, as well as for providing guidance throughout the process of generating the compilation. We also thank the publisher, Springer, and their employees, for progressing this book. Finally, we are really thankful to all the contributing authors who provided the valuable submissions that made this book possible.

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