

Preface

Anticoagulants



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Editor

Anticoagulants have increasingly become a therapeutic mainstay in the management of patients for multiple prophylactic and therapeutic reasons. Warfarin and other vitamin K antagonists (VKAs) are still extensively used for multiple indications and will likely continue to be the agents of choice for patients with valvular heart disease, mechanical heart valves, and ventricular assist devices. However, with the advent of new oral anticoagulation agents (NOACs), newer paradigms for patient management have also emerged. The NOACs provide additional therapeutic approaches to anticoagulation for patients in multiple settings, including inpatient and outpatient, surgical, and medically managed patient populations, as extensively reviewed in this issue.

New pharmacologic agents provide novel approaches for patient management but, as with all therapies, they have associated risk and benefit profiles that must be considered to optimize patient management. For all anticoagulation agents, the major risk is of course bleeding. However, while bleeding can occur with any anticoagulation therapy, there has been increasing attention on NOAC-associated bleeding, as therapeutic approaches for managing bleeding in NOAC-treated patients are different than those validated for use in warfarin-treated patients. Despite widespread criticism that “antidotes” for the NOACs don’t exist, until 2013 there were no four-factor prothrombin complex concentrates available for warfarin/VKA reversal in the United States. Plasma/fresh frozen plasma (FFP) is still widely used despite the fact that the lowest international normalized ratio obtainable with FFP is 1.6,¹ and recent studies have shown that the use of FFP is a leading cause of volume overload.^{2–4} In addition, while the use of male-only plasma has reduced the number of antibody-mediated cases of transfusion-related acute lung injury (TRALI), and associated mortality, TRALI still remains a concern.⁵ Furthermore, despite the ongoing extensive use of low-molecular-weight heparin (LMWH) in surgical patients and in a hospital setting, there is no reversal agent available to treat a life-threatening bleed in LMWH-treated patients.

In this issue of *Clinics in Laboratory Medicine*, the focus is on anticoagulation. For this publication, I have assembled many of the world experts to review and discuss critical aspects of both older and newer anticoagulants and their management, including patient monitoring, evaluating laboratory testing, and evaluating what coagulation test results mean. In addition to discussion on monitoring and managing patients receiving factor Xa and direct thrombin inhibitors, there are extensive discussions on bleeding management in these patients. As part of this important topic, I have included anticoagulation and bleeding management in a spectrum of important settings, including postoperative atrial fibrillation, intracranial hemorrhage, extracorporeal membrane oxygenation, trauma, and perioperative management. The idea for the content of this supplement came in part from a 2013 satellite symposium sponsored by CSL Behring at the International Society of Thrombosis and Haemostasis (ISTH), entitled “Bleeding Emergencies: Strategies for the Reversal of Old- and New-Generation Oral Anticoagulants”; five of the articles were developed from the presentations given at this meeting. I also invited other experts on anticoagulation management, who will share their understanding of management and urgent reversal of anticoagulation in a complex set of in-hospital settings, from adult to pediatrics (extracorporeal membrane oxygenation), in the perioperative setting, and from other therapeutic settings. I have also included an article on understanding the extensive use (and abuse) of prothrombin and partial thromboplastin times in patients as monitoring tools for both anticoagulation and potential bleeding.

The evolution of cardiovascular medicine and therapeutic approaches has been greatly facilitated with the development of multiple pharmacologic strategies for anticoagulation, including both parenteral and oral agents. However, as previously mentioned, all of these agents are associated with a risk of bleeding, and multiple factors can influence bleeding in anticoagulated patients. This supplement on anticoagulation provides an updated and important review of management approaches in this patient population. Of importance is also the development of purified and recombinant factors and factor concentrates to manage complex bleeding paradigms, which will be discussed in several articles, and other agents currently under investigation.

In summary, my view is that *new drugs create new paradigms*. In addition to the new anticoagulation agents, new strategies for monitoring and managing patients are important and are extensively addressed in the 15 articles included in this issue. I would like to thank the authors, who are busy physicians, clinicians, and scientists, for taking the time to write these articles. Dr Steven Shafer once told me that friends don't ask friends to write articles. However, these articles together represent a collective insight from experts who manage anticoagulation and its side effects on a daily basis, who have contributed to our understanding and to the availability of therapeutic agents for both anticoagulation and urgent bleeding management, and who took the time to make their important contributions. I am most appreciative of their efforts. I would also like to thank Dr Michael Thimme, from CSL Behring, whose ongoing vision and support of important educational programs, including our previous symposium at the ISTH meeting, is most appreciated.

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