

INTRODUCTION

The Inevitability of Change

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Unfractionated heparin (UFH) has justifiably been the keystone of rapid anticoagulation for over half a century. In the past 20 years, however, we have witnessed the development and the Food and Drug Administration approval of newer anticoagulants, such as the low-molecular-weight heparins, direct thrombin inhibitors, and a pentasaccharide. In clinical studies these agents have demonstrated either equivalent or superior outcomes when compared with UFH for indications such as the treatment and prophylaxis of venous thromboembolism (VTE) and the management of acute coronary syndromes. In addition, these new agents offer more convenient dosing, minimal or no monitoring, decreased probability for drug errors, and a lower rate of drug-related problems.

Why do we continue to use UFH in our institutions? The answer is obvious: it is cheap. At a time when pharmacy directors manage within a silo-type financial environment, the nominal acquisition cost of UFH provides an attractive line item compared with any of the newer anticoagulation agents. However, we know that the expense of UFH therapy extends beyond acquisition cost and multiplies throughout the entire drug use process. The complete UFH financial picture is significantly affected by the many limitations and issues associated with its use.

As a crude mixture of molecules, UFH's complicated pharmacokinetic profile brings about a need for frequent dosage adjustments and monitoring. It is associated with a labor-intensive and error-prone administration process. Serious drug-related problems, such as heparin-

induced thrombocytopenia and bleeding events, continue to hinder the success of UFH therapy and increase its risk. In addition, UFH has been a leading drug among those associated with errors causing patient harm.

Historic evidence reveals that the use of UFH weight-based nomograms improves therapy. But today, have all institutions using these dosing guidelines identified and validated their own therapeutic laboratory targets? If not, the clinical outcomes of UFH therapy within each institution are questionable and likely suboptimal. The activated partial thromboplastin time, used to monitor UFH therapy, is associated with its own set of issues, further diminishing one's confidence in this anticoagulation option. As a result, due to this seemingly endless list of issues, the economics of UFH becomes as complicated and burdensome as its use. Therefore, has the time come for change? Yes.

Without an industry sponsor catalyzing the standardization of monitoring and resolution of other UFH issues, we will be unable to "fix" UFH quickly enough. As safer, more effective, and more convenient anticoagulants become part of our formularies, institutional practice standards as well as prescribing habits will evolve. Unfractionated heparin, due to its historic place in therapy spanning over 50 years, always will be recognized as the anticoagulant that set the original standard. However, as we advance to a new era of anticoagulation therapy value justification, UFH will remain in textbooks only.

This supplement is based on the proceedings of an expert meeting entitled "Consensus on Contemporary Issues with Unfractionated Heparin: Challenges in Variation and Responsiveness." The contributing authors are part of the Heparin Consensus Group. In the lead article, Drs. Henry Bussey and John Francis provide a pharmacologic overview of UFH and the many limitations encountered with its use in practice today. Next,

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Drs. John Francis and James Groce discuss the challenges associated with the activated partial thromboplastin time as a monitoring parameter and describe alternative, possibly more logical, options. Drs. Steven Deitelzweig and James Groce present past and recent clinical evidence on the use of UFH in the prevention of VTE in medical patients; the efficacy and safety of UFH are compared with those of newer agents.

Treatment options for VTE, as they challenge the UFH standard, are provided by Drs. Edith Nutescu and Maninder Singh-Khalsa. Drs. Thomas Rihn and Jose Diez outline important consequences encountered with the use of UFH in the management of acute coronary syndromes and compare the agent with more optimal anticoagulants. Next, Dr. Paul Dobesh discusses

UFH nomograms and their ability or inability to guide UFH therapy effectively. An overview of UFH drug errors as well as serious drug-related problems is presented by Dr. Cynthia Niccolai and colleagues. Lynn Oertel, an advanced practice nurse, describes the barriers nurses encounter in their efforts to administer UFH therapy in a safe manner. In the final article, Dr. Dobesh discusses UFH economics, beyond the dimension of acquisition cost and into the real world of clinical practice.

These articles are intended to provoke institutions to evaluate their use of UFH across all indications. The time has come for UFH to step aside for safer and more effective, convenient, and value-based anticoagulation alternatives. Change is inevitable.