

Recent Advances in **Anaesthesia and Intensive Care**

This is the latest volume of this very successful and long-established series (previously entitled *Recent Advances in Anaesthesia and Analgesia*) to present a collection of cutting-edge topics for anaesthetists. It has been compiled by some of the world's leading authorities in their subjects and builds on the successful formula of the previous volumes. As the title suggests, these latest volumes have increased the input from the field of intensive care, and the emphasis remains on producing articles of high quality and interest to the reader while providing exceptional value for money.

This volume is a recommended reading for trainee, practising anaesthetists and intensivists at all levels of experience.

Recent Advances in
Anaesthesia and Intensive Care

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Every effort has been made in preparing this book to provide accurate and up-to-date information which is in accord with accepted standards and practice at the time of publication. Although case histories are drawn from actual cases, every effort has been made to disguise the identities of the individuals involved. Nevertheless, the authors, editors and publishers can make no warranties that the information contained herein is totally free from error, not least because clinical standards are constantly changing through research and regulation. The authors, editors and publishers therefore disclaim all liability for direct or consequential damages resulting from the use of material contained in this book. Readers are strongly advised to pay careful attention to information provided by the manufacturer of any drugs or equipment that they plan to use.

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Preface

In this 23rd edition of *Recent Advances in Anaesthesia and Intensive Care*, we bid farewell to our Senior Co-editor Prof. Anthony (Tony) Adams. Tony joined Dr Richard Atkinson for the 15th edition, which appeared in 1985 and has been a co-editor of *Recent Advances* through eight editions over the past 20 years. When Dr Atkinson stepped down as editor, Tony invited Dr Jeremy Cashman to co-edit the 19th edition. Dr Michael Grounds joined the editorial team for the 22nd edition. Tony's drive, enthusiasm and wisdom born of long experience have been in no small measure instrumental in the continuing popularity of the series. Both of the current editors are grateful to Tony for his wise counsel over the years and for his continuing support, even now when he is no longer an editor. We wish him a long, healthy and happy retirement.

The editors are grateful to the many distinguished colleagues from the USA, Europe and the UK who have contributed to this volume. We have endeavoured to include a range of topics in this issue that represent all aspects of anaesthesia and intensive care. The first four chapters present developments in the basic sciences. There is enormous inter-individual variability in the way patients respond to medications. Indeed, adapting to this heterogeneity is part of the 'art' of anaesthesia. Over recent years, huge progress has been made in our understanding of the structure as well as the function of the genome, allowing researchers to explore those genes that express proteins controlling drug action and metabolism. The burgeoning field of pharmacogenomics deals with the various aspects of gene–drug interactions and aims to further elucidate the inherited nature of inter-individual differences in drug disposition and effects. In Chapter 1 *Pharmacogenomics: the genetic basis for variability in drug response*, Dr Sweeney reviews the current status of work in this field, highlights anaesthetic examples and addresses strategies that hold promise for the future; recombinant DNA technology has already resulted in the introduction of

drugs, such as recombinant human activated protein C (Chapter 8) and human insulin (Chapter 9). In Chapter 2 *The opioid receptor and opioid peptides*, Dr Zöllner and Prof. Stein review recent developments in the understanding of opioid receptors. Molecular cloning has had a tremendous impact on our knowledge of the μ -, δ - and κ -opioid receptors, as well as identifying the opioid-like orphan receptor 1 (ORL-1). Cellular mechanisms of action including opioid receptor desensitization (important in the development of tolerance; Chapter 10) and endogenous ligands are discussed. The functional aspects of opioid use with specific reference to their peripheral antinociceptive effect are considered. Normal haemostasis is achieved by a complex mechanism comprising a balance between pro- and anti-coagulant forces. Hereditary or acquired deficiency of factors on either side of this balance may result in a prothrombotic or a haemorrhagic tendency. The system is continually active at a low rate, which allows it to be rapidly responsive to haemorrhagic challenge. Separation of the physiological trigger for coagulation from the effector enzymes in plasma is essential for controlling this system. In Chapter 3 *Coagulation*, Dr Laffan explains how improved understanding allows us to effectively manipulate this system and treat these disorders for therapeutic benefit. It has become apparent that anaesthetic drugs can influence the heart by augmenting or inhibiting (or indeed having no overall effect) on cardioprotective mechanisms. Prof. Schlack and Dr Ebel, in Chapter 4 *Anaesthetic agents and myocardial protection*, point out the evidence that cardioprotection by anaesthetic agents can be elicited in the clinical setting and may add to other organ protection strategies. Volatile anaesthetic agents can interfere with ischaemic preconditioning, may act against reperfusion injury and as a result may impact on patient outcome in ischaemia–reperfusion situations.

The next two chapters deal with trauma and emergency medicine topics. As Drs Gardner and McDonagh state in Chapter 5 *The treatment of heart failure due to left ventricular systolic dysfunction*, heart failure is a serious condition, with a worse prognosis than many forms of cancer, that affects a significant proportion of the population. Until recently, the goal for the treatment of heart failure was to relieve symptoms and enhance functional capacity. However, recent studies have shown that pharmacotherapy with angiotensin converting enzyme inhibitors and β -adrenergic receptor blockade and cardiac resynchronization therapy combined with automatic implantable cardioverter defibrillator implantation can reduce both the morbidity and the mortality of chronic heart failure. Drs Gardner and McDonagh also present the results of recent trials of nesiritide and levosimendan in acute heart failure. Blunt chest trauma remains an extreme clinical challenge, accounting for nearly 25% of all traumatic deaths. Life-threatening chest lesions are frequently associated with extrathoracic

injuries that may contribute to severe, sometimes delayed, cardio-respiratory failure. However, apparently minor trauma may also be life threatening. In Chapter 6 *Blunt chest trauma*, Drs Edouard, Minville and Martin present the management of this condition, including the use of new imaging technology in the assessment of trauma patients. A specific, step-wise therapeutic strategy is outlined.

Two of the primary goals of haemodynamic monitoring are to identify the presence of circulatory shock and to guide specific goal-directed treatments. In Chapter 7 *Functional haemodynamic monitoring* Drs Chavko and Pinsky present recent advances in monitoring techniques and review clinical trials that support the rationale of applying ‘functional’ measures of cardiovascular performance to define specific treatment approaches, rather than just the measurement of static haemodynamic values that may reflect a variety of disease processes and their potential responsiveness to treatments. The limitations of the technique are also presented.

The next three chapters consider intensive care topics. Sepsis is one of the most common disease processes encountered in the critically ill population. Sepsis has been, and continues to be, the subject of vast amounts of research, and sepsis therapeutics in particular is a rapidly advancing field. In Chapter 8 *Sepsis and the use of Xigris®*, Prof. Vincent reviews drotrecogin alfa, a recombinant form of the natural protein activated protein C (Xigris®). Xigris is the first immunomodulating drug to be shown to directly influence outcome in patients with severe sepsis and septic shock. The next chapter presents another approach to the problem of infection, acquired either before or after admission to the intensive care unit (ICU). The purpose of selective decontamination of the digestive tract is to prevent or eradicate oropharyngeal and gastrointestinal carriage of potentially pathogenic micro-organisms, leaving the indigenous flora predominantly undisturbed. In Chapter 9 *Selective decontamination of the digestive tract: why don't we apply evidence in practice?* Drs van Saene, Taylor, Barrett, Lowry and Sarginson review the evidence in favour of selective decontamination and propose a radical rethinking of the philosophy by which antimicrobials are used. In the past, hyperglycaemia was considered to be an adaptive stress response, and a rise in blood sugar in critical illness was only treated when blood glucose levels became excessive. However, a recent study clearly established the beneficial effects of strictly maintaining normoglycaemia in ICU patients. Intensive insulin therapy was associated with a remarkable reduction in mortality of ICU patients, particularly in patients with prolonged critical illness. In Chapter 10 *Glycaemic control and outcome in intensive care*, Drs Mesotten, Vanhorebeek and Van den Berghe discuss the mechanisms for this action and describe a regimen for maintaining strict glycaemic control.

Anaesthesia and postoperative analgesia in patients dependent on psychoactive substances poses special problems. These patients commonly suffer from co-existent medical and psychiatric illness. In Chapter 11 *Substance use disorders and anaesthesia*, Prof. Jage introduces the concept of substance use disorders with central nervous system depressant and stimulant substances. The neural basis of addiction is described and the anaesthetic and analgesic management of patients with substance use disorders and ex-addicts is outlined in detail.

This edition of *Recent Advances* aims to afford practising anaesthetists the opportunity to keep abreast of some of the latest developments in our speciality. In addition, the editors feel that it is important that the present volume addresses the whole scope of our speciality from the laboratory to the operating theatre. We hope that readers not only find the chapters in this issue stimulating and interesting but also agree with this approach.

London
July 2004

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