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PREFACE

It has been almost 15 years since the first reports appeared indicating that adenosine exerted a protective effect in ischemic and reperfused myocardium. Numerous experimental studies have shown that adenosine (both exogenous and endogenous adenosine) delays the onset of ischemic contracture, modulates myocardial metabolism during ischemia, attenuates reversible postischemic ventricular dysfunction (myocardial stunning), and reduces myocardial infarct size. Initial studies on adenosine's cardioprotective effect were based on its ability to stimulate postischemic ATP resynthesis, increase coronary blood flow, and reduce heart rate. Although these actions of adenosine are undoubtedly beneficial to the ischemic/reperfused heart, it now appears that adenosine's cardioprotective effect may be exclusive of these properties.

The immense growth in the number of articles on adenosine cardioprotection in the last several years has been related in large part to the hypothesis that adenosine plays a role in ischemic preconditioning. Ischemic preconditioning is the phenomenon in which a brief period of ischemia (and reperfusion) prior to a more prolonged occlusion reduces myocardial infarct size. This form of myocardial protection has received much interest because ischemic preconditioning has been shown to be the most potent means of reducing infarct size in all animal models thus far tested. In fact prior to studies implicating adenosine's role in ischemic preconditioning, adenosine's infarct reducing effect was not well recognized.

Since 1990, the principal focus of adenosine cardioprotection research has centered on the role of adenosine receptors. It is currently thought that adenosine protects the ischemic heart primarily via the activation of adenosine A_1 receptors located on the cardiac myocytes. There are some reports however that adenosine A_2 receptor activation during reperfusion may reduce the extent of myocardial infarction. Still other reports suggest that adenosine may exert its protective effects via stimulation of an adenosine A_3 receptor subtype. Although the majority of evidence suggests involvement of the A_1 receptor, the intracellular signal transduction pathway(s) responsible for adenosine's beneficial effect in ischemic/reperfused myocardium remains unknown. There is evidence for the involvement of ATP-sensitive potassium (K_{ATP}) channels, however there appear to be species differences. There is also evidence for the modulation of calcium

dependent protein kinase (PKC), however there are also controversies regarding this potential mechanism. There are also some differences between ischemic preconditioning, and treatments with K_{ATP} channel openers and adenosine.

Adenosine is used clinically for terminating supraventricular tachycardia, as a diagnostic tool in coronary imaging, and has been used postoperatively for blood pressure control after heart surgery. There are also recent reports that adenosine may be safely tolerated and a potentially beneficial additive to cardioplegic solutions during open heart surgery in humans. There is even evidence that ischemic preconditioning may occur in humans under various clinical situations.

This book contains chapters from contributors to the first three symposia on "Adenosine, Cardioprotection, and its Clinical Application". All aspects of adenosine cardioprotection and ischemic preconditioning, including potential mechanisms and clinical applications, are discussed by experts in these areas. The reader will find this book to be both an excellent source of information on these topics, as well a guide to future experiments.

The editors would like to thank the contributors for their chapters and the symposia attendees for their interest in these topics. We would also like to thank the sponsors and supporters who made these symposia possible. The editors would also like to express their gratitude to Steve Thomas for his assistance in preparing this book.

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