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The Multiple Inert Gas Elimination Technique (MIGET)

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Foreword

It is a special pleasure to write a foreword for this important book by my colleagues Susan Hopkins and Peter Wagner. There are several reasons for this. One is that Peter joined me at UCSD in 1970 and thus has been a colleague for 47 years. This may not be a record, but it has been an unusually rewarding relationship, and, especially in the early days, we cooperated on many projects. Susan has also been a valuable colleague and incidentally is a talented artist. Perhaps I should add that I have not seen quite so much of Peter recently because he has taken up multitasking and now runs a vineyard that produces grapes for what are expected to be exceptional wines.

But the main reason why this book gives me so much pleasure is that it describes an outstanding advance in understanding ventilation-perfusion ($\dot{V}_A/\dot{Q}$) inequality in diseased lungs. $\dot{V}_A/\dot{Q}$ was my first love in respiratory physiology and still remains dear to me. The first paper that I ever published (in 1957) was on the measurement of $\dot{V}_A/\dot{Q}$ inequality from a single expiration, and oddly enough only a few years ago, we used the same technique to make measurements on astronauts in space. In the period during and after World War II, pulmonary gas exchange was a particularly exciting research topic. Two groups of investigators, Fenn, Rahn, and Otis in Rochester, NY, and Riley and his colleagues at Johns Hopkins, made extraordinary advances. I was so enamored that I spent a sabbatical year with Rahn. In those days, the only possible method of analysis was graphical, and Rahn and Fenn produced a softcover booklet with foldout graphs that was the bible for acolytes. The breakthrough came with the application of digital computing, and this volume is a splendid example of what this can do.

$\dot{V}_A/\dot{Q}$ inequality is a demanding area of analysis. The basic physiology is very simple: the gas exchange that occurs in any single lung unit depends solely on the ratio of ventilation to blood flow. But once one starts to consider $\dot{V}_A/\dot{Q}$ distributions, which typically occur in lung disease, the situation quickly becomes very complicated. The development of the multiple inert gas elimination technique has clarified many aspects of the abnormal gas exchange that occurs in patients with lung disease and also in normal subjects under unusual physiological conditions. The book is not bedtime reading, but the serious student of pulmonary gas exchange will find it enormously stimulating. I believe that it will be a valuable reference book for many years to come.

La Jolla, CA, USA John B. West

Preface

The multiple inert gas elimination technique (MIGET) was born in the early 1970s in John West's UCSD laboratory. Some 45 years later, we have thought to bring together in one place as much detail as we can about the method. Why now? It is the sobering thought that we are not immortal and that a lot of the technical information is hard to find, scattered as it is in the literature. It certainly requires a lot of searching, and even then, those not mathematically inclined would be in doubt as to the completeness of the descriptions. Our vision has therefore been to create a reference source that present and future users of MIGET can utilize to enhance their understanding of its theoretical and practical aspects. We also undertook the daunting task of reading and summarizing the world's literature on all aspects of the method, especially concerning its physiological and clinical applications, or at least the literature in the English language, but even there, we may have missed articles for which we apologize in advance.

While the book is certainly not light reading, each chapter has been written with the reader in mind—so that even if the detailed mathematics are set aside, the principles and approaches used hopefully make sense, especially coupled to the liberal use of figures. We begin with a short history and then move to the basic physiological principles underlying MIGET. These are the very same principles used some 70 years ago by our pioneering gas exchange predecessors—the principle that alveolar gas exchange for any gas follows simple laws of mass conservation. What follows are chapters on the mathematical equations required to make MIGET work: how we convert inert gas exchange data into the ventilation-perfusion distribution. A consideration of helpful physiological constraints that are integrated into the mathematics, a consideration of experimental error, and then a description of the physiological information content of MIGET are included.

The direction then changes to cover the practical laboratory aspects including a number of seemingly minor but yet very important technical issues associated with the core technology—gas chromatography. Coupled to this is a discussion of the data entry process which enables the inert gas concentrations to be processed to yield the ventilation-perfusion distribution.

Finally, we discuss how MIGET has been applied in hundreds of studies around the world to throw light on complex gas exchange processes in health and disease. To keep this section under control, we have grouped outcomes into logical topic areas and confined our editorial opinion on the findings in each case to major observations of likely mechanistic importance. The domain of research here has been extremely diverse—small and large animals (mammals, birds, reptiles), human health and disease, and exercise and environmental stresses—posing us a major challenge to be complete yet not endless.

While this final chapter shows that a great many people have contributed to the development and implementation of MIGET over the past 45 years, there are four individuals in particular without whom MIGET likely would never have been imagined, developed, or applied, and this book is dedicated to them: John West, who supported the development of MIGET for many years; Herb Saltzman (chief of the Duke University hyperbaric chambers), who spent a sabbatical with John in the early 1970s and whose discussions kick-started thinking about the use of inert gases to investigate ventilation-perfusion inequality; John Evans, a UCSD mathematics professor (and physician!) who understood our goals and was absolutely instrumental in writing computer programs that converted our amateurish data processing code into a rigorous, understandable procedure; and Harrieth Wagner, whose decades-long technical skill with the gas chromatograph made the difference between success and failure.

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