

Demystifying Drug Dosing IN OBESE PATIENTS

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Dedication

We would like to dedicate this book to our family and friends, as well as to our mentors for their support throughout our careers.

Brandon R. Shank and David E. Zimmerman

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Foreword

Never before has the need for dosing guidance in obese patients been more relevant for clinicians. With the increasing complexity and role of pharmacotherapy in disease-state management, prevalence of obesity, and diversity of factors, which warrant individualized drug dosing, the demand for tools to assist practitioners has been unmet. *Demystifying Drug Dosing in Obese Patients* is the first text focused on dosing critical and narrow therapeutic index drugs in obese pediatric and adult patients.

Dr. Shank and Dr. Zimmerman are both credentialed practitioners with experience in pharmacokinetics and individualized drug dosing throughout their training and in their current positions. They have engaged outstanding collaborating authors, nationally recognized for their clinical expertise and experience, who summarize the body of evidence that supports practical and concise drug-dosing recommendations. The first chapter discusses pharmacokinetic changes in obesity and methods for measures of weight, obesity, and creatinine clearance. Individual chapters address dosing of antimicrobial agents, anticoagulant and antiplatelet drugs, antiepileptics, antineoplastics, immunosuppressants, and analgesics in obese patients. Separate chapters focus on drug-dosing specifics to obese pediatric patients, obese patients in the intensive care unit, and in patients following roux-en-y gastric bypass and other bariatric surgeries. Dosing recommendations for specific drugs are easy to find, relevant, patient-focused, and fully referenced. Equations and sample calculations provide the reader with examples for clarification and application.

Obese rat models used in research to understand the effects of obesity on pharmacokinetics of drugs were impressive, yet their body sizes seemed too extreme to be relevant to “real-life” patient care. However, practitioners have learned repeatedly over the years that it is indeed necessary to consider obesity-associated alterations in drug disposition to optimize drug therapy for specific patient populations.

Demystifying Drug Dosing in Obese Patients is a timely and welcomed contribution to drug dosing publications. New practitioners and seasoned clinicians need this information; yet until now, no text has focused on drug dosing in obesity and provided specific drug-dosing recommendations for a broad scope of therapeutic areas and patient populations. I applaud the authors for making this valuable resource available.

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Preface

Obesity rates continue to grow at an alarming rate in the United States and worldwide. As we encounter increasing numbers of obese patients, especially morbidly obese patients, it is important for clinicians to have an understanding of the complexities involved in determining the optimal medication dose. Unfortunately, obese patients are often excluded from pharmacokinetic (PK) studies, and currently the Food and Drug Administration does not require drug manufacturers to report on patient weight. This leaves great uncertainty for clinicians whether or not absorption, distribution, metabolism, and excretion are affected and, more importantly, the pharmacodynamics with alterations in efficacy and toxicity. In drugs that use weight-based dosing or the patient's weight in calculations (i.e., renal function or body-surface area), the question arises of which weight to use: actual, ideal, lean, or adjusted body weight. For medications that have fixed dosing, does the drug dose achieve adequate concentrations for the given medication?

This is the first published text to comprehensively summarize the available evidence to assist clinicians for drug dosing specifically in obese patients. The clinical interpretation and application of the material is intended for clinicians to quickly and easily find information with summary bullets and tables. The chapter authors include dose recommendations based on the available literature and recommend which weight to use. There are four levels of evidence (I to IV) with level I being the strongest, represented by controlled studies and level IV being expert opinion. In some instances, a level cannot be assigned due to lack of available evidence. In these situations, we recommend following dosing found in package labeling and/or guideline recommendations, as well as the drug's PK characteristics. In every setting, clinical judgment should always be used when applying literature from the population to individual patients and scenarios.

We gathered experts with clinical expertise and experience in their respective areas to evaluate the literature with the goal of bridging the published evidence from controlled studies to give the reader insight on how to apply to real-life scenarios.

This text begins with an overview of dosing medications in patients that are obese, explaining the concepts of absorption, distribution, metabolism, and clearance. Subsequent chapters are then divided by medication topic (i.e., infectious disease, oncology, critical care, pediatrics, and so forth) and include a description and evaluation of the available literature. The last chapter evaluates the literature in patients with bariatric surgeries and the effect on medications. A summary table of recommendations can be found at the end of each chapter, which includes the medications discussed along with the corresponding level of evidence. Following each section of medications in the chapter, there is a short summary at the end along with helpful tips that clinicians should keep in mind when managing patients. Throughout the chapters, there are also example calculations that are designed to help the reader understand the equations.

We want to thank all of the coauthors for their hard work as well as the staff at ASHP who worked tirelessly to develop this book. Without them, this publication would not be possible.

Brandon R. Shank and David E. Zimmerman

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