

Essentials of Pharmacology for Anesthesia, Pain Medicine, and Critical Care

Alan David Kaye
Adam M. Kaye
Richard D. Urman
Editors

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Adam and I wish to thank our parents, Florence Feldman and Joel Kaye, for their love and support. We also want to thank our stepparents, Andrea Kaye and the late Gideon Feldman, along with the Gittelman family for always helping and treating us with love and kindness over our lifetime. All three of us wish to thank Dr. Jonathan Jahr and Dr. Karina Gritsenko, MD, for their extra help in the preparation of this book. This book has been the largest project I have undertaken in many decades. I wish to dedicate this book to everyone interested to learn about anesthesia and pharmacology. I also wish to dedicate this book to my family: my wife Dr. Kim Kaye, my son Aaron, and my daughter Rachel. I also wish to thank my pharmacology and anesthesia mentors, Dr. Alan W. Grogono, MD; Dr. Philip J. Kadowitz, PhD; and Dr. Bobby D. Nossaman, MD, for allowing me to complete my PhD in pharmacology while serving my full-time duties at Tulane Medical Center many years ago.

Alan D. Kaye, MD, PhD

I would like to dedicate this book to my wife Beth Kaye and daughter Jessica Kaye and thank them from the bottom of my heart for their patience and love. I would like to thank James W. Blankenship, PhD, Emeritus Professor, Department of Physiology and Pharmacology, for stimulating my interest while a student at the Thomas J. Long School of Pharmacy and Health Sciences, University of the Pacific. Most importantly, I would like to thank my older and wiser brother Alan Kaye for being my first teacher and best friend.

Adam M. Kaye, PharmD

This book covers extensive amount of material highly relevant to the practice of anesthesiology, pain, and critical care medicine. I would like to thank my colleagues, students, and mentors for encouraging me to undertake this massive project. I hope that current and future generations of practitioners and trainees will benefit from my efforts. I would like to thank my wife Zina Matlyuk, MD, for her editorial assistance and advice. I wish to dedicate this book to Zina, my daughters Abigail and Isabelle, and my parents Dennis and Tanya Urman.

Richard D. Urman, MD, MBA

Foreword

The word *pharmacology* is derived from the Greek φάρμακον, *pharmakon*, and -λογία, *-logia*, “study of.” Strangely φάρμακον meant “poison” in classic Greek but came to mean “drug” in the modern language. But what is a drug? It can be described as anything manufactured, natural, or endogenous that exerts some physiological cellular. Pharmacology is the study of the interactions between a living organism and substances that have an impact on normal or abnormal function.

The division between food and herbs is somewhat blurred as the latter preparations are not governed by the Food and Drug Administration but rather held to the standards of the food industry where trials of effectiveness and universal testing of safety are not required. However, the word “drug” is believed to originate from an old French word “drogue” and later from the Dutch “droge-vate,” which referred to the drying or preserving barrels used to store plants for medicinal use (in other words, drugs and herbs are the same thing). Indeed, today about 30 % of our medicines derive directly from herbs, the only difference being that drugs have specified amounts of active ingredients and herbs are not regulated as to content.

Some of our earliest medical texts have centered on medicinal therapies. The *Yellow Emperor’s Classic of Internal Medicine*, collected around 2600 BC, describes plants and foods that are applicable to the maintenance of health and the treatment of specifically diseased organs. Writing in the first century AD, Pedanius Dioscorides (circa 40–90 AD), a Greek physician, pharmacologist, and botanist, authored a 5-volume encyclopedia about some 600 herbal medicines that was the standard reference for 1,500 years. During the Renaissance the book was read in Latin, Greek, and Arabic. Before that, in the seventh century AD, Paulus Aeginata, also Greek, in a monumental act of plagiarism (although he does give some acknowledgements), collected all the works of Hippocrates, Galen, Dioscorides, and Aretaeus, among others, and produced seven books, the last of which is over 600 pages long and is devoted entirely to herbal remedies. In all of these works, many of the drugs we use today such as opium, aspirin, cannabis, castor oil, mandragora (atropine, scopolamine), cocaine, physostigmine, and digitalis among many others are listed. It is to the efforts of William Withering to understand the effects of this last herb, digitalis, from the purple foxglove, that we see the foundations of pharmacology. In his text,

An Account of the Foxglove, Withering relates how he achieved the potion from an old lady in Shropshire and sent samples to his colleagues to gauge under which circumstances the extract would relieve lower extremity edema and other signs of heart failure.

One of the frightening experiences the new resident in anesthesia has is encountering the sometimes bewildering array of medications that can take patients to the door of death and then (hopefully) bring them back. With an aging population come more comorbidities and the risk of drug interactions increases. Ever-increasing complexity of machines, requirements for monitoring, and mandated data collection all add to the stress of the perioperative period. The ability to turn to a concise yet easy to read comprehensive text on the drugs we use daily is something to be treasured and an immense help for the practitioner. In this, the latest of a long line of pharmaceutical texts, Drs. Kaye and Urman are to be congratulated on gathering together such a wide range of authors from many different venues and perspectives. The coverage of topics within *Essentials of Pharmacology* is indeed encyclopedic. It is my hope that this book will allow practitioners of anesthesia to embrace the topic of pharmacology and thus gain confidence in the knowledge that their patients will be cared for appropriately and safely.

New York, NY, USA

Elizabeth A.M. Frost, MD

Preface

In many academic papers that we have read and written over the years, drugs are described in abstract and theoretical ways. These drugs might possess novel mechanisms or improved duration of activity. These agents might be less toxic or possess reduced side effects. Clearly, drugs dramatically affect our life spans, including our quality of life. As the years have gone by, we have a much greater appreciation for their wonders.

It was not long ago that our life spans were much shorter. Tens of thousands of people died due to plague, an organism easily treated with sulfonamides. It is an astonishing fact that dysentery was the single greatest cause of death of Confederate and Union soldiers during our epic Civil War. Some of our greatest figures in history had shortened lives related to what we would now consider very treatable states. George Washington probably died of acute bacterial epiglottitis. The poet Lord Byron died prematurely from an epileptic seizure. Harry Houdini probably died from acute appendicitis. Arthur Ashe died, in part, from transmission of the human immune deficiency virus. Thousands of people die each year from NSAID-mediated silent gastrointestinal bleeding.

Principally during the last 50 years, we have dramatically increased our understanding of disease states, and the technology to detect these states has also grown significantly. Drug development has resulted in an increasing longevity, reduced pain, and enhanced quality of life. On a daily basis in every community, an anesthesiologist is called to a code with a patient appearing lifeless and without hope and delivers atropine, epinephrine, sodium bicarbonate, and calcium, and the patient is ultimately rescued and stabilized. These drug-mediated miracles are commonplace and routine in our practices.

In the last decade, we have seen complete cataloging of the entire human genome and an increase in drug targets from five hundred to well over one thousand. No longer is it a guaranteed death sentence to have human immune deficiency virus, many types of cancers, or sepsis. There is now new hope in drug targeting for vascular atherosclerosis, diabetes mellitus, cardiomyopathy, many cancers, and even Alzheimer's disease. We find ourselves constantly at a new beginning with drugs, including in our fields of anesthesia and pain medicine. Structural activity

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