

Preface

The physician's oath begins with a commitment to risk reduction—*primum non nocere*. The physician's responsibility also includes the fundamental duty to relieve suffering whenever possible. Opioids are a powerful and dangerous tool in the therapeutic armamentarium. Much like the homesteader's chainsaw or the miner's dynamite in the Last Frontier where I reside, opioids can accomplish much in the short term, although untrained and indiscriminate use invites disaster. As with most decisions in medicine, opioid therapy involves ongoing risk-benefit ratio analysis. At the beginning of the twenty-first century, we are in a position to better evaluate previously underappreciated risks and potentially overstated benefits (of chronic opioid therapy).

At an individual level, we are seeing prevalent recalcitrant (and likely increased) chronic pain and depression and dysfunction associated with chronic opioid use. We are becoming aware of immunosuppressive and endocrinopathic effects of this drug class that have not yet made it into standard pharmacology textbooks. We are being told that more people die today in America from opioid overdose than from automobile accidents. And unlike many other intervention decisions the physician must make, there are societal "ripple effects" of chronic opioid therapy. Opioids prescribed by even the best-informed and best-intentioned clinicians are diverted into the wrong hands. No other therapeutic intervention (besides benzodiazepines) even comes close to sharing the public health liability of opioids.

This book is intended to "bring the practitioner up to speed" on:

- Opioid basic science
- Current areas of drug improvement research and development
- Alternatives to opioid therapy
- Evidence-based indications for opioid therapy
- Evidence-based indications against opioid therapy
- Clinical strategies for preventing and overcoming opioid dependence

Part I of the book provides an overview comparing (and contrasting) classic infectious disease epidemiology concepts with what has been labeled the opioid epidemic in America. A paradigm categorizing our current understanding of basic

science and best clinical practices in terms of agent (opioid), vector (prescriber), and host (patient) factors is offered. The remainder of the book is organized according to these three arenas.

Part II of the book is devoted to understanding the agent and potential means of attenuating its “virulence.” Chapter 2 surveys the current state of our basic science knowledge concerning opioids. While attempting to be as comprehensive as possible in scope (under the constraints of maintaining clinical relevance), no single work can survey the vast research into opioids that has amassed over the past half century. Every decade brings more answers into mechanisms of action that beget more questions. The complexity of opioid receptor activity on an enormous array of biochemical processes is only beginning to be unraveled. Heteromerization of receptors with alterations in function and effect and regulatory interactions between these receptors and other systems are apparently protean. Traditional concepts of pharmacokinetics and pharmacodynamics are constantly being revised by new understanding of these interdigitating systems and also by pharmacogenetics which confer another level of clinical variance altogether.

Chapter 3 examines the adverse effects (or “harms” as they are increasingly described as in the literature) of various opioids, organized by physiologic systems. A literature review of opioid adverse effects follows, based upon recent systematic reviews.

Chapter 4 presents agent-specific pharmacology for the commonly prescribed opioids in America (arranged in alphabetical order). While the generalist certainly does not need to be an expert in all of the agents available, the growing scope of the problem of opioid abuse in this country necessitates some familiarity with all of the commonly used agents, regardless of specialty. The old injunction to “know a few agents really well” is certainly reasonable; however, staying abreast of the current knowledge base is essential when prescribing potentially lethal agents and those that can otherwise ruin a life.

Chapter 5 looks at historic, current, and potential future means of altering currently available drugs and adjunctive therapies—attenuating agent virulence—to reduce the risks of adverse effects, especially as they pertain to psychological and physical dependence and addiction.

Part III of the book examines the vector, and while the entire book is obviously intended to educate prescribers about best clinical practices, this section focuses on presenting guidance to providers for reducing their contribution to the epidemic or attenuating vector transmission.

Chapter 6 introduces the section with a primer on acute and chronic pain assessment and treatment. It is not intended to serve as a textbook on pain; vast works (e.g., Bonica’s, Waldman’s, Deer’s) provide excellent resources for pain management and other specialists and generalists. This chapter is intended to provide a scaffold for thinking about pain which (despite aggressive campaigning to label as a disease in its own right) remains a symptom, and a cardinal one at that, for many underlying pathologic states—including emotional and cognitive disturbance. It also offers a brief survey of multimodal approaches to explore with patients or consult with colleagues in other specialties.

Chapter 7 discusses *why* (or *why not*) and *when* (or *when not*) to prescribe opioids. An initial discussion of acute pain, and the special situation of postoperative pain (which increasingly represents “acute-on-chronic” pain), is followed by an evaluation of the evidence for or against opioid therapy for chronic pain. Currently available systematic reviews examining the efficacy of chronic opioid therapy are organized by categories of both “nociceptive” pain and neuropathic pain. Finally, a survey of both national and international clinical practice guidelines on opioid therapy for cancer pain is presented.

Chapter 8 presents *how* to prescribe opioids, arranged by regulatory and advisory oversight. Federal and state laws are discussed, followed by a synthesis of recommendations from the major current national clinical practice guidelines on opioid therapy, arranged loosely to follow the well-established Federation of State Medical Boards’ Model Policy.

The book’s final section is centered on an attempt to better understand and prevent opioid misuse and dependence in the host population—our patients and their families and associates.

Chapter 9 begins with a review of addiction theories. Choice and compulsion models are compared and contrasted in an effort to illuminate these complex self-destructive human behaviors that science will likely never fully explain nor address. An introduction to social models of addiction follows. The chapter closes with a brief acknowledgment that the understanding of motivation lies at the heart of comprehending addiction.

Chapter 10 examines specific risk factors for opioid use disorder/addiction based upon current research and also presents guidance on risk assessment when considering opioid therapy. The more commonly used standardized clinical instruments are discussed along with a literature review of their validation. This is followed by a brief overview of compliance/aberrancy monitoring using standardized and validated questionnaires and urine drug testing.

Chapter 11 concludes this section on addressing host factors—likely the most important and difficult to effectively intervene upon in this epidemic—arranged by the common public health schema of primary, secondary, and tertiary prevention. Primary prevention will most effectively occur if we are able to confer “behavioral immunity,” i.e., reducing or eliminating the desire to seek and use the drug. Negative motivation includes education as to the risks and diminishing benefits of opioid use. Enlightening patients that pain is not in fact their worst enemy, but biologically and teleologically perhaps the most important protective sense we possess, is vital to overcoming disproportionate focus on and dread of pain, with potentially escalating sensitization and/or hyperalgesia (which is often accelerated by opioid use). Positive motivation includes promotion of healthy lifestyle choices, non-opioid pain management options, and above all self-efficacy. The environment comprises a crucial and to this point unaddressed component of the standard “epidemiologic triangle” and is introduced in this section.

Secondary prevention assumes that the process can be reversed. Education is not confined to primary prevention. It has been said that there are two things that will reliably bring people into the physician’s office—bleeding and pain. If we can

convince the patient that chronic opioid use in most situations is worsening their pain (via opioid-induced hyperalgesia, depression, and overall health reduction), we may achieve more risk reduction than attempting to convince them about morbidity and mortality. As a sidenote, while I still preach cardiovascular, pulmonary, and oncologic risk reduction as more than adequate reasons for smoking cessation, increasingly, I appeal to data showing that cigarettes increase pain; patients seem to care more about that issue oftentimes. Opioid weaning and a brief introduction to Rollnick and Miller's motivational interviewing techniques are introduced.

Tertiary prevention is traditionally equated with damage control, but I do not hold the completely pessimistic viewpoint that "once an addict, always an addict." Despite the discouraging statistics on relapse, there are too many success stories from people who have decided that there is something they want more than voluntary slavery to a substance—be that alcohol or oxycodone—and have sought and found the help they need in achieving recovery and abstinence. An overview of clinical practice guidelines from the American Society of Addiction Medicine, with its biopsychosocial-spiritual "multidimensional assessment" focus, is given, along with a discussion of medication-assisted treatment, organized by the three currently FDA-approved pharmacotherapeutics (methadone, buprenorphine, and naltrexone). The chapter concludes with an examination of evidence and recommendations for overdose education and naloxone distribution.

Each of the chapters in Parts II through IV begins with a case study, some of which are drawn from the author's practice and some from the literature or popular news. Josef Stalin reportedly once said that the death of one man is a tragedy, while the death of millions is a statistic. While espousing none of his political viewpoints, this quote serves to remind us that the epidemic we face and the strategies and policies we implement affect individual human beings as well as our nation.

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Opioid Dependence

A Clinical and Epidemiologic Approach

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2018, XV, 301 p. 22 illus., 16 illus. in color., Hardcover

ISBN: 978-3-319-47496-0