patients with advanced cancer. Although this textbook is focused on symptom management in advanced cancer, the guidelines can be used for similar symptoms found in other advanced diseases, making it a great addition to the libraries of all palliative medicine specialists.

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Opioid Use in Cancer Pain Management

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Opioids in Cancer Pain, 2nd ed.
Edited by Mellar P. Davis, Paul Glare, Columba Quigley, and Janet R. Hardy
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The second edition of this book offers an international treatment of the use of opioids for cancer pain. Columba Quigley of the United Kingdom has been added as part of the editorial team, and both Paul Glare and Janet Hardy of Australia offer their expertise as both editors and authors. Mellar Davis from the United States completes the intercontinental triad of editors who provide a global perspective on how to use opioids in malignant disease.

This edition presents new insights into opioid pharmacology and organ failure while adding underaddressed topics such as opioids in pediatrics and developing countries, addiction and cancer pain, the use of buprenorphine, opioids in terminal conditions, and the more complex but intriguing topic related to the pharmacogenetics of opioids. Many chapters include evidence from the literature for opioid use among noncancer pain patients and applications for use among special populations (e.g., older adults and pediatric populations). There is some content overlap in the chapters; however, the relevant evidence base for cancer pain provided within each subject matter stresses the theme of educating the reader on the importance of opioids in alleviating cancer pain. There is mixed value for clinicians according to chapter. That is, many chapters are weighted heavily toward the pharmacokinetics and pharmacodynamics of opioids and provide fewer practical guidelines for the palliative care specialist, oncologist, or pain medicine specialist. However, the text is written clearly, and certain tables offer excellent summaries of helpful data for patient assessment or treatment with opioids. A summary of each chapter with distinctive features of the subject follows.

Chapters 1–4 review opioid pharmacology. For example, Chapter 1 highlights the pharmacodynamics of opioids and reminds the reader of the wide diversity of opioid responses requiring individualized therapy. Several sections focus on the molecular basis of opioid receptors and their actions. The authors do not specifically correlate cancer pain with changes in the pharmacodynamics of opioids. Chapter 2 provides a short description of opioid pharmacokinetics and offers the clinician an overview of absorption, distribution, metabolism, and excretion. Very little information is specific to cancer pain, however. The authors note that pharmaceutical manufacturing has provided sustained-release dosage formulations that promote more effective analgesia and patient compliance. Tables on long-acting opioids, pharmacokinetic variables for opioid analgesics, and opioid metabolites are especially useful for the clinician. Chapter 3 describes the substantial pharmacokinetic alterations to opioids that occur during liver disease, with useful recommendations for clinical use. Yet, there is minimal reference to cancer pain specifically in this chapter. Chapter 4 provides very useful clinical guidance on the use of opioids in renal failure, with some correlation to cancer conditions. Tables covering causes of renal failure in cancer patients and the effect of dialysis on opioids are especially relevant for the practitioner.

The editors dedicate Chapters 5–17 to profiling specific opioids that are often used internationally to ease cancer pain. For instance, Chapter 5 provides a concise discussion of

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codeine for clinical use mostly as a combination medication with acetaminophen and refers to specific studies in cancer pain. Chapter 6 highlights hydrocodone and emphasizes its singular availability as a compounded analgesic with ibuprofen or acetaminophen. Chapter 7 offers a profile of tramadol ranging from its pharmacology, use in special populations, and then to its evidence base for effectiveness in cancer pain. Chapter 8 gives a good overview of the international use of dextropropoxyphene (propoxyphene) for cancer pain despite the few studies supporting its effectiveness. The authors mention that many experts believe that the potential for adverse effects outweigh propoxyphene's benefits among older adults. Chapter 9 provides the clinician with useful information on the pharmacology of morphine, drug interactions and toxicity, including hypogonadism and immunosuppression, and guidelines for the appropriate and practical use in cancer pain based on the evidence. Chapter 10 informs the reader of the pharmacology of oxycodone, drug interactions of this opioid, use in special populations (e.g., liver failure, renal failure, and the elderly), and provides the evidence base for effectiveness in reliving cancer pain. Chapter 11 describes the pharmacological and clinically relevant properties of the lipophilic opioids: fentanyl, alfentanil, sufentanil, and remifentanil. There is some attention to their use in cancer pain, but more discussion of studies in the noncancer pain population exists. Chapter 12 provides a good overview of the pharmacology of buprenorphine, clinical situations favoring its use, and many studies supporting its application among cancer patients. Chapter 13 provides a comprehensive description of methadone pharmacology, highlights pertinent drug interactions including a useful table, explains its cardiac toxicity, and provides brief descriptions of its use in managing cancer pain. The authors provide additional information on methadone's perioperative use and principles of conversion. Chapter 14 notes that hydromorphone for cancer patients is currently included among clinical practice guidelines although there exists great heterogeneity in study design and outcome measures. Chapter 15 reports on the paucity of the evidence base for the use of levorphanol in cancer pain, whereas the author feels that it is underused and forgotten because of the development of sustained-release preparations of other opioids. Levorphanol binds to multiple opioid receptors, including kappa receptors, which selectively reduce visceral pain in humans.

Chapter 16 reports on the use of diamorphine (heroin) as an analgesic. This opioid is used principally in the United Kingdom for chronic cancer pain but not elsewhere because of concerns about abuse and addiction. Most experts believe that no difference in analgesic efficacy between morphine and heroin exists. Finally, chapter 17 highlights oxymorphone pharmacology and the limited evidence base for its application in cancer pain. New immediate-release and extended-release formulations were introduced to the United States market in 2006. It is not available in the United Kingdom or Australia.

Chapter 18 reviews the value of the World Health Organization (WHO) ladder for cancer pain control and suggests alternate approaches that may provide more comprehensive management. Comparative costs of opioids in developed vs. developing nations also are presented.

Chapter 19 provides a rather detailed and technical examination of current pharmacogenetic data associated with opioid analgesic response and adverse effect profiles. Several studies are summarized that investigate opioid metabolism, receptors, and drug transporters. This represents a more recent area of investigation; therefore, further developments are necessary for a more complete understanding of how genes influence a person's response to opioids.

Chapter 20 considers the benefits of opioid rotation. There is no strong evidence that one drug is superior to another, and all opioids produce similar adverse effects and analgesic efficacy but with great interindividual variability. Therefore, clinicians should consider alternative opioids (i.e., "opioid rotation") when confronted with inadequate analgesia or intolerable side effects based on abundant clinical experience suggesting that opioid switching is beneficial.

Chapter 21 emphasizes the intrinsic and extrinsic factors influencing equianalgesia. The authors note that equianalgesic tables do not account for a multitude of factors, such as differences in opioid metabolism, pharmacogenetics, organ function, aging, and drug interactions. Some specific suggestions on opioid switching are particularly helpful for the clinician.

Chapter 22 includes dosing strategies for acute pain. Discussions about opioids for acute noncancer pain and options for acute pain in

cancer are offered, with a section devoted to postoperative pain in opioid-tolerant cancer patients. The authors do provide helpful strategies when using opioids to control acute pain.

Chapter 23 reiterates the WHO guidelines, discusses the causes and treatment options for breakthrough pain, and provides clinically useful recommendations for treating opioid-related side effects.

Chapter 24 details the use of patient-controlled analgesia (PCA), including the history of its use, problems, management, strategies for dosing, and a systematic review of PCA use in cancer patients. Overall, pain control is improved, but the authors conclude that there is probably a small advantage of PCA over traditional parenteral dosing.

Chapter 25 offers a good review of the neuroanatomy and pharmacology of spinal opioids followed by some strategies for using opioids and nonopioids for cancer pain control. A limited treatment of intrathecal pumps is provided along with comparative data on epidural vs. intrathecal delivery. There are few studies on the use of implantable drug delivery systems or spinal opioids for cancer pain that are presented.

Chapter 26 discusses the concepts of physical dependence and tolerance, with a focus on forms of tolerance. Opioid poorly responsive pain and opioid-induced hyperalgesia are also mentioned.

Unique features of this text relate to considerations of opioids in special populations. Specifically, Chapter 27 highlights the special needs of developing countries in providing opioids for cancer pain and palliative care. Global access to pain relief is poor, but three countries (India, Romania, and Uganda) are moving toward greater access to morphine for those in need. Chapter 28 offers a good description of opioid use in children along with available evidence for specific opioids in pediatric cancer pain. Pediatric pharmacology of minor and major opioids and recommendations for prescribing opioids in children are discussed. Chapter 29 reiterates the value of opioids at the end of life and reminds the clinician that several studies support the use of opioids for terminal care without hastening death. Chapter 30 provides an understanding of commonly misunderstood terms, such as tolerance, abuse, and addiction. It reassures the clinician that opioid therapy in chronic cancer pain patients without a history of abuse or addiction can be undertaken with very low risk. Simultaneously, the chapter offers broad guidelines on the approach to opioid use for those patients with medical illness (e.g., cancer pain) who have a history of substance abuse.

In summary, the second edition of this text is primarily applicable to three groups of specialists: pharmacists, oncologists, and palliative care experts. The text presents extensive data on the pharmacology of opioids and, therefore, represents an excellent resource for pharmacists and students of opioid pharmacology and toxicology. Clinicians will find Chapters 18–26 relevant and helpful in their practice of prescribing opioids for those suffering from cancer pain. Targeted data on specific opioids found in Chapters 5–17 serve as a useful compendium for oncologists, pain medicine specialists, and palliative care physicians. All pain practitioners should consider incorporating into their treatment algorithm the suggestions provided in the final chapter that focuses on the use of opioids for cancer patients with coexisting substance abuse.

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End-of-Life Care for the Critically Ill

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For the novice or expert nurse, nurse practitioner, physician or social worker in the hospice,

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