

# Understanding Opioid Tolerance in Cancer Pain

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**Purpose/Objectives:** To review opioid tolerance in chronic cancer pain, define the phenomenon and its scope, review physiologic mechanisms, and discuss clinical strategies to identify and manage this complex issue.

**Data Sources:** Review articles, case studies, original research, and published guidelines.

**Data Synthesis:** Novel therapies to prevent/reverse tolerance are being investigated with a possible future role for N-methyl-D-aspartate antagonists.

**Conclusions:** Greater nursing research is needed to identify patient risk factors for tolerance development and clinical measurement of the phenomenon. Understanding cellular mechanisms for tolerance may contribute to better management.

**Implications for Nursing Practice:** Nursing knowledge of tolerance is important to provide the basis for accurate patient assessment, education, and pain management.

Managing chronic cancer pain can be a complex and overwhelming experience for many healthcare providers, particularly if opioid tolerance is involved. The multifaceted aspects of this phenomenon and compound layers of psychosocial, physiological, societal, and legal dimensions surrounding narcotic use complicate the main objective of providing the most appropriate intervention for individuals to successfully treat their pain. Oncology, home health, and hospice nurses frequently are involved in identifying and assessing changes in pain status, patient and family counseling/education, and ongoing reevaluation and management of pain control. This article attempts to define the phenomenon of tolerance and its scope, demystify the physiology behind it, and discuss clinical strategies to identify and manage this complex issue.

## Definitions

To discuss the clinical implications of opioid tolerance, understanding what is meant by tolerance and other related phenomena is necessary. **Tolerance** is defined as a physiologic phenomenon of progressive decline in the potency of an opioid with continued use, manifested by the requirement of increasing opioid dose to achieve the same therapeutic effect (Ferrante et al., 1996). This definition assumes that the

## Key Points . . .

- Advances in the understanding of tolerance development and physiology of tolerance (particularly the role of the N-methyl-D-aspartate receptor) may lead to novel therapies to prevent or reverse its development; however, with the prospect of considering tolerance prevention comes the need to more accurately define tolerance, its incidence, and the characteristics of the population at risk.
- Current strategies to reverse opioid tolerance include changing to an alternate opioid (e.g., methadone), altering the route (e.g., oral to parenteral or epidural), and attempting opioid-sparing strategies (e.g., adding nonsteroidal anti-inflammatory drugs, tricyclic antidepressants), or nerve blockade when appropriate.
- In attempting to study opioid tolerance and effective interventions, a great need exists for accurate strategies to measure this phenomenon and more consistent operational definitions are needed to meaningfully interpret outcomes across studies.

## Objectives for CE Enrollees

- On completion of this CE, the participant will be able to
1. Describe etiology associated with opioid tolerance development.
  2. Describe characteristics related to opioid tolerance.
  3. Describe some of the physiologic mechanisms associated with opioid tolerance.

pain stimulus and perception of pain remain constant. Clinically, this may be difficult to distinguish from another closely related phenomenon of opioid-induced **hyperalgesia**, in which exaggerated sensitivity to noxious stimuli occurs (Mao, Price, & Mayer, 1995). Hyperalgesia may mimic tolerance

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