

Meeting the Challenges of Managing Patients With Complex Pain Syndromes

Part of the *INROADS into Pain Management Series*

Sunday, September 13, 2009

Hyatt Regency Jacksonville Riverfront

Jacksonville, Florida

19th Annual ASPMN National Conference

Seeing Pain Management in a New Light

AMERICAN SOCIETY FOR
**Pain Management
Nursing**

This educational activity is sponsored by the
American Society for Pain Management Nursing.

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Activity Description

Optimal pain management is accomplished when nurses understand the complexity of pain, conduct comprehensive pain assessments, and apply rational therapies based on scientific evidence. Mixed pain syndromes arise from more than one, and sometimes multiple, pathophysiological explanations for pain. Patients with mixed pain syndromes present unique assessment and treatment challenges. This interactive symposium examines the peripheral and central mechanisms for neuropathic pain, wind-up, and central sensitization, and rationale for targeted pharmacotherapy to manage and treat chronic mixed pain syndromes.

Learning Objectives

Upon completion of this activity, participants should be able to:

- Describe the physiology of pain and pathophysiology mechanisms (peripheral and central) for complex mixed pain syndromes and presentations
- Understand differential assessments to evaluate patients with mixed pain and response to therapy
- Apply critical thinking and utilize clinical decision making to manage and treat patients with mixed pain
- Evaluate scientific information and incorporate evidence-based practice strategies in the treatment of mixed pain with multimodal therapies

Intended Audience

Pain management nurses and other health care professionals who manage pain.

Agenda

- The Physiology of Pain
 - Rosemary C. Polomano, RN, PhD, FAAN, Chair
- Complex Pain: Differential Assessments to Evaluate Mixed Pain
 - Colleen J. Dunwoody, MS, RN-BC
- Complex Pain: Considerations for Assessment and Management
 - Chris Pasero, MS, RN-BC, FAAN
- Multimodal Pain Therapy
 - Rosemary C. Polomano, RN, PhD, FAAN, Chair
- Panel Discussion and Questions and Answers
 - Moderated by Rosemary C. Polomano, RN, PhD, FAAN, Chair

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Accreditation



This continuing nursing education activity has been submitted to the New York State Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation (ANCC). This educational activity is offered for a maximum of 1.5 ANCC.

Commercial Support



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Chair

Rosemary C. Polomano, RN, PhD, FAAN
Associate Professor of Pain Practice
University of Pennsylvania School of Nursing
Associate Professor of Anesthesiology and Critical Care (Secondary)
University of Pennsylvania
Philadelphia, Pennsylvania

Faculty

Colleen J. Dunwoody, MS, RN-BC
Advanced Practice Nurse
University of Pittsburgh Medical Center Presbyterian
Pittsburgh, Pennsylvania

Chris Pasero, MS, RN-BC, FAAN
Educator and Clinical Consultant
El Dorado Hills, California

Disclosure Statement

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Faculty Disclosures

The following speakers have a financial interest or affiliation with manufacturer(s) of products, devices, or services discussed in this activity.

Colleen J. Dunwoody, MS, RN-BC

Does not have any relevant financial relationships with a proprietary entity that produces health care goods and/or services consumed by, or used on, patients.

Chris Pasero, MS, RN-BC, FAAN

Consultant: Alpharma Inc.; Baxter Healthcare; Endo Pharmaceuticals; Ortho-McNeil-Janssen Pharmaceuticals, Inc.

Speakers Bureaus: Baxter Healthcare; Cardinal Health; Ortho-McNeil-Janssen Pharmaceuticals, Inc.

Rosemary Polomano, RN, PhD, FAAN, Chair

Consultant: Merck & Co. Inc.; Ortho-McNeil-Janssen Pharmaceuticals, Inc.

Speakers Bureaus: Merck & Co. Inc.; Ortho-McNeil-Janssen Pharmaceuticals, Inc., Wyeth Pharmaceuticals



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About the Faculty

Rosemary C. Polomano, PhD, RN, FAAN, Chair

Associate Professor of Pain Practice

University of Pennsylvania School of Nursing

Associate Professor of Anesthesiology and Critical Care (Secondary)

University of Pennsylvania

Philadelphia, Pennsylvania

Rosemary C. Polomano, RN, PhD, FAAN, received her bachelor of science in nursing and master of science in nursing from the University of Pennsylvania School of Nursing, in Philadelphia, and earned her PhD from the University of Maryland School of Nursing in 1995. She began her career as a staff nurse at the Hospital of the University of Pennsylvania, later assuming positions as an advanced practice nurse in oncology and pain management.

In 1998, after completing a postdoctoral fellowship in laboratory research at Hahnemann University, Philadelphia, Dr. Polomano accepted a position at the Penn State Hershey Medical Center and College of Medicine to pursue a Career Development Award from the National Institute of Nursing Research, investigating Taxol-induced peripheral neuropathy in rats. There, she advanced to the positions of Director, Outcomes Research, Department of Nursing, and Associate Professor in the Department of Anesthesiology at the Penn State College of Medicine. She returned to the University of Pennsylvania in August 2004.

Dr. Polomano has participated in several national advisory boards and has been involved in many initiatives to improve pain management. She has lectured throughout the country on pain-related topics, including the assessment and management of pain in long-term care. She has been involved with numerous research projects and has authored or co-authored more than 50 peer-reviewed articles and 30 book chapters in nursing and medical textbooks.

Dr. Polomano serves on the editorial board for the international journal *Clinical Therapeutics and Pain Medicine*, and is a reviewer for several peer-review professional journals. She has been the recipient of numerous scholarships, including the United States Pharmacopeia Scientific Fellowship Award, the American Cancer Society's National Doctoral Fellowship Scholarship, and the University of Maryland Graduate School's Merit Award for Scholastic Academic Achievement. Dr. Polomano has also received national research awards for her investigations related to acute and chronic pain management.



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Colleen J. Dunwoody, MS, RN-BC

Advanced Practice Nurse

University of Pittsburgh Medical Center Presbyterian

Pittsburgh, Pennsylvania

Colleen J. Dunwoody, MS, RN-BC, received her nursing diploma from Presbyterian-University Hospital School of Nursing, her bachelor of arts in sociology from the University of Pittsburgh, and her master of science from the University of Pittsburgh School of Health Related Professions, with a concentration in education. She is

the advanced practice nurse for pain management at the University of Pittsburgh Medical Center (UPMC) Presbyterian Shadyside, where she has held positions as staff nurse, head nurse, and clinical instructor. She is certified by the American Nurses Credentialing Center in pain management nursing.

Ms. Dunwoody is a past president of the American Society for Pain Management Nursing, past president of the board of directors of the American Chronic Pain Association, and served as the advisor and the site coordinator for Thunder Project II, a multicenter collaborative clinical research study conducted by the American Association of Critical-Care Nurses. She serves on both the Ethics, Pharmacy, and Therapeutics Committee and the Adverse Drug Events Committee of the University of Pittsburgh Medical Center and Co-chairs the Pain Management Council.

She has served as a member of the editorial board of *Orthopaedic Nursing and Pain Management Nursing*, published on a variety of topics in *Orthopaedic Nursing, RN, Nursing Clinics of North America, AORN Journal, Nursing, Dermatology Nursing, Congress Reporter, and Joint Commission Journal on Quality and Patient Safety*, and written a number of book chapters. In addition, she has given presentations both regionally and nationally.

Ms. Dunwoody has received considerable recognition for her contributions to the nursing profession. Her awards include the 2005 University of Pittsburgh School of Nursing Cameo of Caring Award for Advanced Practice Nursing, American Society of Pain Management Nurses Clinical Practice Award, Presbyterian-University Hospital Hall of Fame Award, University of Pittsburgh Medical Center Service Excellence Achievement Award, and the Outstanding Alumna Award from the Presbyterian-University Hospital School of Nursing Alumnae Association. The project team under her leadership was awarded the UPMC Presidential Quality Improvement Award in 2001 for "Promoting Safe Use of Patient Controlled Analgesia."



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Chris Pasero, MS, RN-BC, FAAN

Educator and Clinical Consultant

El Dorado Hills, CA

Chris Pasero, MS, RN-BC, FAAN, is a nationally recognized pain management author, educator, and clinical consultant from El Dorado Hills, California, who specializes in helping healthcare facilities improve pain assessment and management. She earned her master of science in nursing from California State University in Sacramento.

Ms. Pasero is a co-founder and past president of the American Society for Pain Management Nursing and serves on the board of directors of the American Chronic Pain Association. She is a Fellow in the American Academy of Nursing, board certified in pain management nursing, and the recipient of numerous pain management clinical practice, journalistic, and teaching awards, including the American Pain Society's Elizabeth Narcessian Award for Outstanding Educational Achievements in the Field of Pain.

Ms. Pasero serves on the editorial boards for *Nursing Consult*, *Federal Practitioner*, *Journal of Medical Case Reports*, *Pain Management Nursing*, and the *Journal of PeriAnesthesia Nursing*. In addition to numerous pain management articles, position papers, guidelines, and book chapters, her publications include the second edition of *Pain: Clinical Manual* and the soon-to-be-released, *Pain: Assessment and Pharmacologic Management*.

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Welcome and Introduction

Rosemary C. Polomano, RN, PhD, FAAN, Chair
Associate Professor of Pain Practice
University of Pennsylvania School of Nursing
Associate Professor of Anesthesiology and Critical Care (Secondary)
University of Pennsylvania
Philadelphia, PA

Complex Concepts Nurses Need to Understand

- Pathophysiological mechanisms of pain
- Challenges of opioid tolerance
- Differential assessment of opioid-induced hyperalgesia
- Multimodal therapy

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Physiology of Pain

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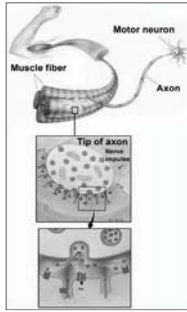
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Nociceptive Pain – Somatic

- Pain resulting from activation of nociceptors in the cutaneous (skin and underlying tissues) or deep tissues such as bone, blood vessels, muscles, and other supporting structures
 - Deep Somatic Pain

Pain syndrome examples

- Traumatic bone fractures
- Muscle sprains
- Post-op incision pain



Galer B, Gammatori A, Alvarez N. 6. Immunology [XIV. Pain]. In: Dale DC, Federman DD, eds. *WebScientific American Medicine*. New York, NY: WebMD Corporation; 2003.

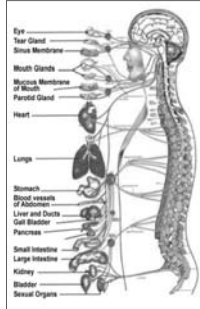
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Nociceptive Pain – Visceral

- Activation of nociceptors in the organs and linings of the body cavities capable of responding to stimuli caused by stretching, inflammation, or ischemia of visceral structures

Pain syndrome examples

- Pancreatitis
- Hepatic Metastases
- Irritable Bowel Syndrome



Galer B, Gammatori A, Alvarez N. 6. Immunology [XIV. Pain]. In: Dale DC, Federman DD, eds. *WebScientific American Medicine*. New York, NY: WebMD Corporation; 2003.

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Neuropathic Pain

- Pain believed to be sustained by aberrant somatosensory processing in the PNS or CNS
 - “Centrally mediated”
 - Deafferentation pain (eg, phantom pain)
 - Sympathetically maintained pain (eg, complex regional pain syndrome [CRPS])
 - “Peripherally mediated”
 - Originate in the nerve root, plexus, or nerve
 - Polyneuropathies and mononeuropathies

Galer BS, Dworkin RH. *A Clinical Guide to Neuropathic Pain*. New York, NY: McGraw Hill, Healthcare Information Programs; 2000:8-9.

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Complex Pain: Definitions

- Complex pain presentations often involve “mixed pain”^{1,2}
- The term “mixed pain” is generally applied to pain with underlying pathophysiology characterized by combinations of nociceptive and/or neuropathic pain^{1,2}
 - Somatic and visceral pain
 - Somatic and neuropathic pain
 - Visceral and neuropathic pain
 - Somatic, visceral and neuropathic pain

1. Portenoy RK, et al. *J Pain*. 2006;7:583-91.
2. Webster LR. *Am J Manag Care*. 2008;14(5 Suppl 1):S116-22.

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Mixed Pain

- Mixed pain includes^{1,2}:
 - Specific pain syndrome such as fibromyalgia, headache syndromes, and low back pain
 - Specific disease states such as cancer or AIDS
 - Presentations of pain caused by multiple etiologies, eg, cancer-related pain and postherpetic neuralgia (PHN)
 - Mixed neuropathic pain is characterized by both peripherally and centrally mediated pain, eg, stump pain from amputation and phantom limb pain

1. Portenoy RK, et al. *J Pain*. 2006;7:583-91.
2. Webster LR. *Am J Manag Care*. 2008;14(5 Suppl 1):S116-22.

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Challenges Associated With Mixed Pain

- Delineating the multiple physiological and pathophysiological sources of pain^{1,3}
- Assessing sites and sources of pain through subjective and objective criteria^{1,2}
- Implementing evidence-based multimodal treatment approaches¹
- Preventing and managing adverse effects from combination pharmacological therapies^{1,2}
- Knowing when to refer patients to pain management specialists³
- Mixed pain often requires multimodal treatment strategies³

1. Portenoy RK, et al. *J Pain*. 2006;7:583-91.
2. Webster LR. *Am J Manag Care*. 2008;14(5 Suppl 1):S116-22.
3. Crews JC. *JAMA*. 2002;288:629-632.

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Complex Pain: Differential Assessments to Evaluate Mixed Pain

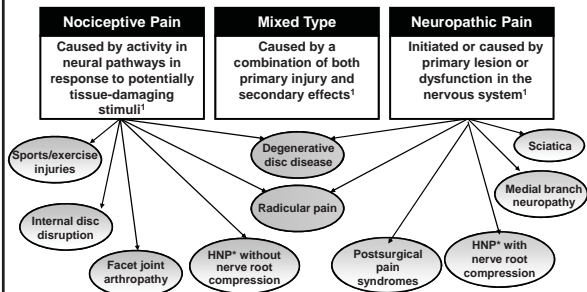
Colleen J. Dunwoody, MS, RN-BC
University of Pittsburgh Medical Center Presbyterian
Pittsburgh, PA

Clinical Case: Chronic Lower Back Pain (CLBP)

- Mr. L is a 46-year-old man with history of CLBP, type 2 diabetes, and osteoarthritis
- Presents with an acute episode (onset 1 day prior) of low back pain
- Body mass index (BMI): 38
- History of depression (currently taking sertraline)

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Possible Nociceptive vs Neuropathic Components of LBP



¹ Portenoy RK, Karner RM. Definition and Assessment of Pain. In: Portenoy RK, Karner RM, eds. Pain Management: Theory and Practice. Philadelphia, Pa: FA Davis Company; 1996:4.

*Herniated nucleus pulposus

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Clinical Case: CLBP

History

- **Current pain status**
 - Intermittent unilateral pain in the left leg with radiating weakness to the foot
 - Intensity ranges from 5/10 to 9/10
- **Health history**
 - Moderate osteoarthritis in the knees
 - Moderate CLBP for approximately 5 years after an automobile accident
- **Medication history**
 - Increasing doses of extended-release oxycodone over past year
 - Diclofenac sodium topical gel 4 g qid to each knee
 - Oxycodone extended-release 80 mg q12h with short-acting oxycodone 15 to 30 mg every 3 to 4 hours as needed

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Clinical Case: CLBP

Initial Assessment

Current Status

- Currently patient presents with unrelieved intermittent unilateral radiating pain down the left leg and increased pain in both knees from osteoarthritis
- Mr. L is insisting that doses of his opioids be increased as he cannot stand the pain
- He reports that he is tired of being on disability and wants to have a better quality of life

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Clinical Case: CLBP

Initial Assessment

DISCUSS AND DECIDE...

Identify the possible pathophysiological mechanisms for his pain

Why is this patient not achieving adequate pain relief with his opioid regimen?

- a) Opioid-nonresponsive neuropathic pain
- b) Opioid tolerance
- c) Worsening depression
- d) Opioid hyperalgesia
- e) Aberrant drug-seeking behaviors

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Clinical Case: CLBP

Is the answer...?

a. Opioid-nonresponsive neuropathic pain

- Initiated or caused by a primary lesion in the nervous system manifesting as intermittent unilateral pain in the left leg
- Requires steadily increasing doses of opioids in order to obtain relief

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Opioids and Neuropathic Pain

Examples: morphine, oxycodone, fentanyl

- Remain therapeutic mainstay for moderate to severe pain management¹
- Most common agents in the class act at the mu receptor¹
- Agonistic effects both in peripheral nociceptors and centrally (spinal cord and descending pathway)¹
- Prescribed as part of multimodal and interdisciplinary treatment plan²
- Some severe chronic neuropathic pain conditions can be successfully managed with opioid therapy^{3,4}
- Considerations
 - Past history of drug or alcohol abuse
 - Low starting dose
 - Dosing spread around the clock and not prn



1. Brunto LL, Lazo SS, Parker KL, Goodman & Gilman's The Pharmacological Basis of Therapeutics, 11th ed. New York, NY: McGraw Hill; 2006.
2. Kalso E, et al. *Current Medical Research and Opinions*. 2005; 21(11): 1521.
3. Celer SS. *Neurology*. 1996;46(suppl 8):S22.
4. Galer B, Gammalioni A, Alvarez N, & Immunology [XIV. Pain]. In: Dale DC, Federman DD, eds. *WebScientific: American Medicine*. New York, NY: WebMD Corporation; 2003:2054.

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Clinical Case: CLBP

Is the answer...?

b. Opioid tolerance

- Decreased response to a drug dosage requiring a higher and higher dose to obtain the same effectiveness

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Is This Patient Developing Tolerance or Is Pain Worsening?

- Opioid tolerance is a “shift to the right” in the dose-response curve

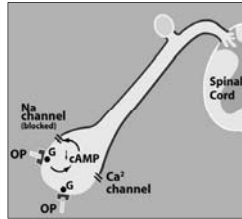
- Higher dose required over time to maintain the same level of analgesia

- Tolerance can be pharmacokinetic...

- Drug or concomitant medications upregulate metabolic pathways that remove opioids from the body

- ...or pharmacodynamic

- Desensitization
 - Physiological changes to the opioid receptors
- Downregulation
 - Internalization of opioid receptors by endocytosis, reducing their numbers



DuPen A. *Pain Manag Nurs*. 2007;8:113-121.

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Clinical Case: CLBP

Is the answer...?

c. Worsening depression

- Pain may be a sign of depression

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Is Depression Worsening? LBP ↔ Psychological Factors

- Prolonged back pain may be associated with a psychological disturbance, manifesting as¹⁻³:

- Behavioral
- Cognitive
- Affective
- Somatoform (psychophysiological)

- Psychological factors that may contribute to or be caused by chronic LBP include^{1,2}:

- Depression
- Anxiety
- Somatization
- Posttraumatic stress disorder
- Preexisting bipolar or other disorders

1. Anderson GB. *Lancet*. 1999;354:581-585.
2. Anderson GB. The epidemiology of spinal disorders. In: Frymoyer JW, ed. *The Adult Spine: Principles and Practice*. 2nd ed. 1997.
3. Polatin PB, et al. *Spine*. 1993;18:66-71.

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Social Issues May Contribute to CLBP

- Job dissatisfaction/loss of ability to work
- Pursuit of disability compensation
- Substance abuse
- Family dynamics
- Financial issues
- Loss of social identity or context
- Loss of ability to participate in recreational activities

Wheeler AH, Stubbart JR. Pathophysiology of chronic back pain. <http://emedicine.com/neurotopic516.htm>.

28

Clinical Case: CLBP

Is the answer...?

d. Opioid-induced hyperalgesia

- Diminished tolerance for pain following opioid administration, which results from changes to the nervous system

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Could This Patient Have Opioid-induced Hyperalgesia (OIH)?

- Increased sensitivity to pain resulting from opiate administration
- Opioids, in addition to providing analgesia, can set in motion anti-analgesic or hyperalgesic processes
- Pain-free animals made tolerant to morphine have significantly decreased tolerance to pain¹
- Opioid "tolerance" may not be a downregulation of analgesic systems, but an upregulation of hyperalgesic systems²

1. Compton MA. Pain Symptom Manage. 1994; 9:462-473.
2. Laulin JP, et al. Neuroscience. 1999;89:631-636.

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Treatment Strategies for LBP

Clinical Presentation	Possible Cause of LBP	Treatment Strategies
Axial, aching, throbbing, and/or stabbing LBP with trigger points radiating to buttocks and anterior thigh	Inflammation of surrounding tissue or joint, myofascial	<ul style="list-style-type: none"> • NSAIDs • Opioids • Topical analgesics
Pain > expected from injury, burning, electrical, to one or both limbs, edema, mottling, nail, skin, and hair changes, temperature change, allodynia, hyperalgesia	Sympathetically maintained pain	<ul style="list-style-type: none"> • Opioids • TCAs • Anticonvulsants • Topical analgesics

Moskowitz MH. *Curr Pain Headache Rep.* 2003;7:178-187.

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Role of Opioids With Chronic LBP

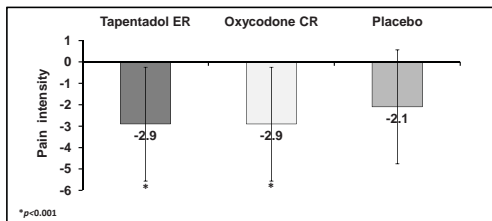
- Opioids have a role in the management of chronic back pain¹
 - American Pain Society and American Academy of Pain Medicine concluded that chronic opioid therapy can be effective treatment with chronic noncancer pain²
 - 2009 AGS guideline recommends that all geriatric patients with moderate to severe pain, pain-related functional impairment or diminished quality of life due to pain be considered for opioid therapy³

1. Kelso E, et al. *Curr Med Res Opin.* 2005;21:1819-1828.
 2. Chou R, et al. *J of Pain.* 2009;10:113-130.
 3. AGS Panel on Persistent Pain in Older Persons. Pharmacological Management of Persistent Pain in Older Persons. American Geriatrics Society. *J Am Geriatr Soc.* 2009.

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Tapentadol ER: Effective in CLBP

- Compared with placebo, tapentadol ER significantly reduced pain intensity
- Tapentadol ER provides comparable pain relief to oxycodone



Buyrak R, et al. Presented at: American Pain Society's 28th Annual Scientific Meeting, 2009. Poster 301.

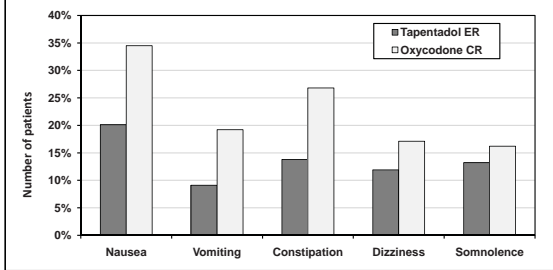
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Tapentadol ER: Improved Tolerability

Incidences of Treatment-emergent Events for Tapentadol ER and Oxycodone CR



1. Elropohl M, et al. Presented at American Pain Society's 28th Annual Scientific Meeting, 2009. Poster 306.
2. Buynak R, et al. Presented at American Pain Society's 28th Annual Scientific Meeting, 2009. Poster 301.
3. Buynak R, et al. Presented at American Pain Society's 28th Annual Scientific Meeting, 2009. Poster 293.

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Designing an Effective Treatment Plan for Mr. L

- Initial treatment plan
 - Continue current opioid regimen (avoid escalating doses)
 - Complete opioid treatment agreement
 - Initiate NSAID while monitoring renal function
 - Initiate topical analgesic
 - Provide patient education (body mechanics, maintaining activity)
 - Schedule physical therapy

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Designing an Effective Treatment Plan for Mr. L

- Reevaluate after 2 weeks
 - If no improvement, consider initiating multimodal therapy
- Reevaluate after an additional 2 weeks
 - If no improvement, add additional modality
 - Consider tapering opioid in the presence of OIH



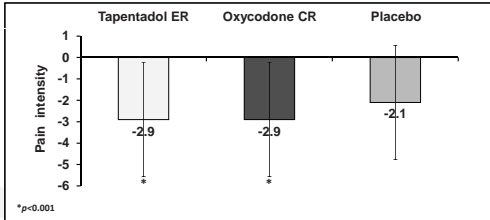
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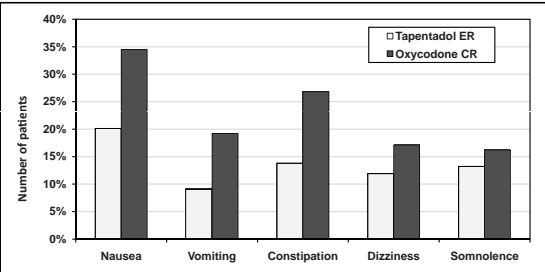


Buyrak R, et al. Presented at: American Pain Society's 28th Annual Scientific Meeting, 2009, Poster 301.

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Tapentadol ER: Improved Tolerability

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1. Etropolski M, et al. Presented at: American Pain Society's 28th Annual Scientific Meeting, 2009, Poster 306.
2. Buyrak R, et al. Presented at: American Pain Society's 28th Annual Scientific Meeting, 2009, Poster 301.
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Designing an Effective Treatment Plan for Mr. L

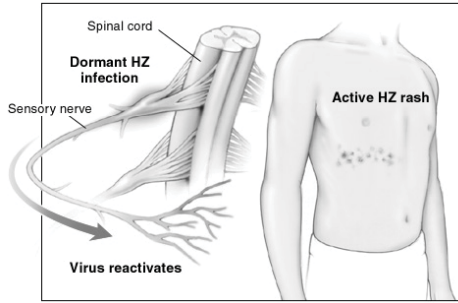
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Schematic of Varicella Zoster Virus (VZV) Latency and Reactivation



Adapted from <http://merck.micromedex.com/images/bhg/BHG01D10F02.gif>.

HZ = Herpes Zoster

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Clinical Case: Breast Cancer Initial Assessment

DISCUSS AND DECIDE...

Patient reports excruciating pain in her torso and upper arms

What type of pain is she experiencing?

- a) Chronic cancer pain (somatic and visceral in origin)
- b) Postherpetic neuralgia (PHN)
- c) Cutaneous hypersensitivity (allodynia and hyperalgesia)
- d) All of the above

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Chronic Pain From PHN

- Significant pain or dysesthesia that persists for 3 or more months¹
- Risks are greater with higher baseline pain severity and older age¹
- 63% to 70% report pain 1 year after herpes zoster infection²

¹ Dworkin RH, Portenoy RK. Pain 1996;67:241-251.
² Watson CP, et al. Neurology. 1998;50:1837-1841.

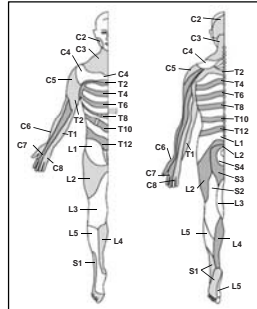
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Typical Locations of Herpes Zoster

- 56% thoracic
- 13% lumbar
- 13% cranial
- 11% cervical
- 4% sacral
- 3% other sites



Raggozzino MW, et al. *Medicine (Baltimore)*. 1982;61:310-316.

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Characterization of Pain Associated With PHN

- **Dysesthesia:** an unpleasant abnormal sensation, spontaneous or evoked¹
- **Hyperalgesia:** pain of exaggerated severity in response to normally painful stimulation¹
- **Allodynia:** pain evoked by a normally innocuous stimulus¹
 - Allodynia in some patients with PHN is a form of chronic secondary hyperalgesia maintained by input from intact and possibly “irritable” primary afferent nociceptors to a sensitized CNS²

1. Merskey H, Bogduk N. *Classification of Chronic Pain*. 2nd ed. Ann Arbor, Michigan: IASP Press; 1994:209-214.

2. Petersen KL, et al. *Pain*. 2000;88:125-133.

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PHN: Risk Factors

- Age
- Severity of acute pain
- Severity of acute rash
- Painful prodrome
- Gender – Female

Jung B. *Neurology*. 2004;62:1545-1551.

Dworkin R, et al. *J Infect Dis*. 1998;178:576-580.

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Meeting the Challenges of Managing Patients With Complex Pain Syndromes

Part of the *INROADS into Pain Management Series*

Underlying PHN Pain Mechanisms and Clinical Presentation

- Both peripheral and central pathophysiological mechanisms contribute to PHN pain
- Some patients with PHN have abnormal sensitization of cutaneous nociceptors (irritable nociceptors)
 - Such patients characteristically have minimal sensory loss
- Some patients have pain associated with small fiber deafferentation
 - Pain and temperature sensation are profoundly impaired
 - Light mechanical stimuli can often produce severe pain (allodynia)
 - Allodynia may be due to abnormalities in peripheral and central pain transmission
- Other patients with deafferentation have severe spontaneous pain without hyperalgesia or allodynia
 - Pain is likely due to increased spontaneous activity in deafferented central neurons and/or reorganization of central connections

Fields HL, et al. *Neurobiol Dis.* 1998;5:209-227.

55

Assessment of Neuropathic Pain

- Examination
 - Tactile sense
 - Vibration sense
 - Heat/cold
- Pain assessment tools
 - Short-form McGill Pain Questionnaire
 - Neuropathic Pain Questionnaire
 - Brief Pain Inventory (BPI)

Crucchi G, Traini A. *PLoS Med.* 2009;6:1-6.

56

Management Strategies for PHN

Therapy	Limitations
Lidocaine 5% patch	<ul style="list-style-type: none">• Erythema or rash• Caution in patients receiving class I antiarrhythmics
Antidepressants	<ul style="list-style-type: none">• Anticholinergic AEs, sedation, cardiac conduction abnormalities
Anticonvulsants	<ul style="list-style-type: none">• Somnolence, dizziness, gait disturbances, gastrointestinal (GI) upset
Opioid analgesics	<ul style="list-style-type: none">• CNS- and GI-related AEs
Dual-mechanism agents	<ul style="list-style-type: none">• Similar to opioids but with better GI profile

AEs = adverse effects

Kost R, et al. *N Engl J Med.* 1996;355:32-42.

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Meeting the Challenges of Managing Patients With Complex Pain Syndromes

Part of the *INROADS into Pain Management Series*

Clinical Case: Breast Cancer Treatment Plan

DISCUSS AND DECIDE...

How would you manage this patient's PHN?

- a) Lidocaine 5% patch
- b) Opioid analgesics
- c) Tricyclic Antidepressants (TCAs)
- d) Anticonvulsants
- e) Multimodal therapy

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Management of PHN

- **Topical lidocaine**
 - Start therapy at onset of pain
- **Antidepressants (eg, nortriptyline, desipramine, duloxetine)**
 - Blocks reuptake of norepinephrine (NE) and/or serotonin
 - Oral dose given at onset of pain
- **Anticonvulsants (eg, gabapentin, pregabalin)**
- **Opioids (eg, mu agonists)**
- **Dual mechanism agents (tramadol, tapentadol)**

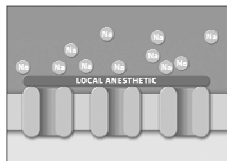
Koss R, et al. *N Engl J Med*. 1996;355:32-42.

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Classes of Pain Medications: Local Anesthetics

Examples: lidocaine, bupivacaine

- **Modulate sodium channels**
- **When administered peripherally, may produce differential—also known as sensory—block**
 - Interrupts some nerve conduction, but leaves motor function unaffected
 - Some nerves are more readily blocked than others, depending on size and myelination
- **Interrupts pain input at the nerve roots**
- **Associated with few adverse effects**



Brunton LL, Lazo SS, Parker KL, Goodman & Gilman's *The Pharmacological Basis of Therapeutics*, 11th ed. New York, NY: McGraw Hill; 2006.

60

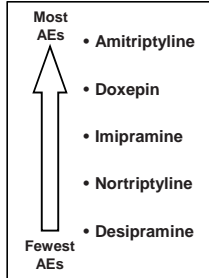
Meeting the Challenges of Managing Patients With Complex Pain Syndromes

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Tricyclic Antidepressants: Adverse Effects

• Commonly reported AEs (generally anticholinergic):

- Blurred vision
- Cognitive changes
- Constipation
- Dry mouth
- Orthostatic hypotension
- Sedation
- Sexual dysfunction
- Tachycardia
- Urinary retention

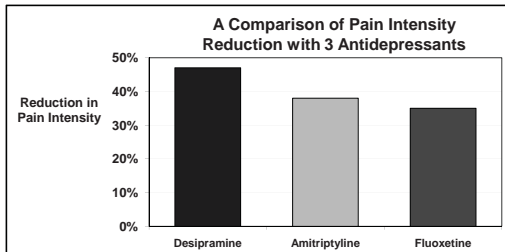


Brunton LL, Lazo SS, Parker KL, Goodman & Gilman's *The Pharmacological Basis of Therapeutics*, 11th ed. New York, NY: McGraw Hill, 2006.

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Antidepressant Use for PHN

- 2005 study revealed that TCAs and Selective serotonin reuptake inhibitors (SSRIs) reduced PHN pain, with desipramine providing satisfactory relief in 80% of those treated



Rowbotham MC. *J Pain*. 2005;6:741-748.

65

Classes of Pain Medications: Anticonvulsants

Examples: gabapentin, pregabalin, lamotrigine

- Decrease excitability of neurons by modulating sodium channels; do not act on gamma-aminobutyric acid (GABA)
- Emerging as top-line adjunct in acute pain and first-line therapy in chronic pain
- AEs/limitations
 - Most common adverse effects are CNS related, including sleepiness, dizziness, and fatigue



Brunton LL, Lazo SS, Parker KL, Goodman & Gilman's *The Pharmacological Basis of Therapeutics*, 11th ed. New York, NY: McGraw Hill, 2006.

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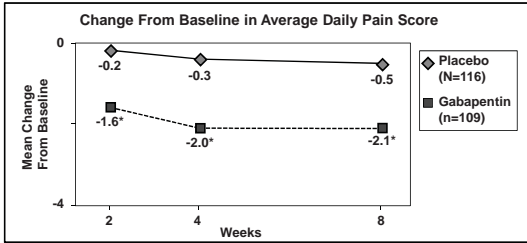
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A Study of Gabapentin for PHN

Outcome

- Gabapentin was effective in relieving pain in patients with PHN
 - Average daily pain score was significantly reduced compared with the placebo



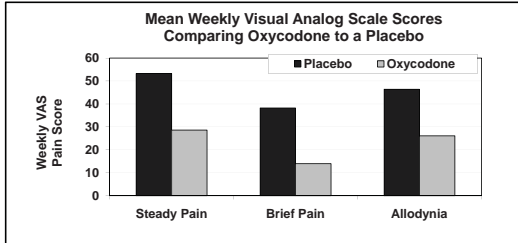
Rowbotham M, et al. JAMA. 1998;280:1837-1842.

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Study of Controlled-release Oxycodone in PHN

Outcome

- Controlled-release oxycodone is an effective analgesic for the management of steady pain, paroxysmal spontaneous pain, and allodynia, which frequently characterize PHN



Watson CP, Babul N. Neurology. 1998;50:1837-1841.

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Managing Complex Pain Syndromes

- Perform a comprehensive pain assessment
- Consider multimodal therapy
- Acknowledge barriers to pain care

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Meeting the Challenges of Managing Patients With Complex Pain Syndromes

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Treatment Plan and Outcome for Mrs. M

- **56-year-old breast cancer patient with PHN**
 - After weighing treatment options, the patient was eventually treated with multimodal therapy
 - Continue current opioid therapy
 - Oral gabapentin for systemic analgesia
 - Topical lidocaine for local relief
 - The patient recovered comfortably over the next 3 weeks

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Multimodal Pain Therapy

Rosemary C. Polomano, RN, PhD, FAAN

Medication Therapy of Chronic Pain: an Evolving Understanding

- **Recognizing the need for a multimodal approach to medication therapy**
 - Combinations of medications and techniques that target more than 1 pain mechanism, not 2 medications that target the same one
 - Not a new concept, but one that is gaining increasing attention as a therapeutic framework
 - Strong evidence to support the utility of this approach; incorporated into major pain management guidelines
 - American Pain Society¹
 - American Society of Regional Anesthesia and Pain²
 - American Society of Anesthesiology³

1. Gordon DB, et al. *Arch Intern Med*. 2005;165:1574-1580.

2. Rathwell JP, et al. *Reg Anesth Pain Med*. 2006;31:1-42.

3. American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology*. 2004;100:1573-1581.

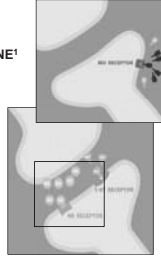
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Meeting the Challenges of Managing Patients With Complex Pain Syndromes

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Moving to a Multimodal Strategy: Dual-mechanism Analgesics

- A single medication with dual mechanisms of action
 - First in class: tramadol
- Newest dual-mechanism agent is tapentadol
 - Acts on mu opioid receptors and inhibits reuptake of NE¹
 - Available in Immediate Release (IR) formulation
 - Clinical trial experience
 - Comparable to oxycodone in acute pain (bunionectomy)² and in more chronic pain (up to 90 days in joint or back pain)³
 - Comparable or better pain relief than morphine in dental surgery⁴
 - Main adverse effects similar to conventional opioids (GI, CNS), but significantly better GI profile, including lower rate of constipation⁵
 - May be associated with less tolerance¹
 - May be useful in patients with opioid sensitivity



1. Tzschentke TM, et al. *Drugs Future*. 2006;31:1053-1061.
2. Oh C, et al. Presented at: American Pain Society's 27th Annual Scientific Meeting, 2008. Abstract 229.
3. Oh C, et al. Presented at: American Pain Society's 27th Annual Scientific Meeting, 2008. Abstract 226.
4. Klenert R, et al. *J Pain*. 2006;7:14 suppl 21:S44. Abstract 773.
5. Hartnick C, et al. Presented at: American Pain Society's 27th Annual Scientific Meeting, 2008. Abstract 222.

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Moving to a Multimodal Strategy: Dual-mechanism Analgesics

- Tapentadol ER: emerging extended-release formulation
 - Acts on mu opioid receptors and inhibits reuptake of NE¹
 - Demonstrate efficacy and safety in:
 - Moderate to severe chronic pain due to osteoarthritis of the knee²
 - Chronic low back pain. Comparable with oxycodone in pain intensity relief with improved GI tolerability^{3,4,5}
 - Management of chronic neuropathic pain in patients with diabetic peripheral neuropathy⁶
 - Better gastrointestinal tolerability compared with oxycodone²⁻⁵



1. Tzschentke TM, et al. *Drugs Future*. 2006;31:1053-1061.
2. Raysoglyb C. Presented at: American Academy of Pain Medicine 24th Annual Meeting, 2008. Abstract 159.
3. Etropolski M, et al. Presented at: American Pain Society's 28th Annual Scientific Meeting, 2009. Poster 306.
4. Buynak R, et al. Presented at: American Pain Society's 28th Annual Scientific Meeting, 2009. Poster 301.
5. Buynak R, et al. Presented at: American Pain Society's 28th Annual Scientific Meeting, 2009. Poster 293.
6. Etropolski M, et al. Presented at: American Diabetes Association 69th Scientific Sessions, 2009. Abstract 852-P.

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Drug Therapy of Chronic Pain: Implications for Future Practice

- Multimodal therapy will continue to evolve through use of novel agents and technologies
 - Dual-mechanism agents
- Increased knowledge of the physiology of pain and pharmacotherapy helps nurses safely and effectively understand and administer multimodal analgesia
 - Focused assessments and reassessments
 - More consistent and reliable dosing to reduce analgesic gaps
 - More options to advocate for individual patient's treatment needs

Polomano RC, et al. *Pain Manag Nurs*. 2008;9:S33-41.

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Meeting the Challenges of Managing Patients With Complex Pain Syndromes

Part of the *INROADS into Pain Management Series*

Multimodal Strategy: Implications for Nursing Practice

- **Effective and safe practices with multimodal strategies require that nurses:**
 - Understand the rationale for combining analgesics^{1,2,4}
 - Be knowledgeable about classes of analgesics^{1,2,4}
 - Mechanisms of action and pharmacodynamics
 - Synergistic and AEs
 - Ensure timely administration of all analgesics, avoiding gaps in analgesia²⁻⁴
 - Institute proper assessment and monitoring practices^{2,3}
 - Aggressively manage AEs of analgesics^{1,2,4}
 - Remain informed about novel dual-mechanism analgesics and drug delivery systems^{1,2,4}

1. Krenzschek DA, et al. *Pain Manag Nurs*. 2008;9:522-32.

2. Durwoody CJ, et al. *Pain Manag Nurs*. 2008;9:511-21.

3. Polomano RC, et al. *Pain Manag Nurs*. 2008;9:53-10.

4. Polomano RC, et al. *Pain Manag Nurs*. 2008;9:533-41.

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When Should Patients Be Referred to a Pain Management Specialist?

- **Complex pain syndromes**
- **Unsuccessful outcomes**
- **Multimodal therapy**
- **History or pre-existing substance abuse**
- **Problems with adherence**
- **Interventional procedures**
- **Behavioral or cognitive therapy**

Chou R, et al. *J Pain*. 2009; 10:113-130.

80

Suggested Reading List

1. AGS Panel on Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. American Geriatric Society. *J Am Geriatr Soc*. 2009 (in press).
2. Chou R, et al. Opioid treatment guidelines: clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J of Pain*. 2009;10:113-130.
3. Compton, P. The OIH paradox: can opioids make pain worse? Pain treatment topics. <http://pain-topics.org/pdf/Compton-OIH-Paradox.pdf>. August 20, 2008. Accessed July 14, 2009.
4. Cruccu G, Truini A. Tools for assessing neuropathic pain. *PLoS Med*. 2009;6:1-5.
5. Dunwoody CJ, et al. Assessment, physiological monitoring, and consequences of inadequately treated acute pain. *Pain Manag Nurs*. 2008;9:S11-21.
6. DuPen A. Mechanism of opioid-induced tolerance and hyperalgesia. *Pain Manag Nurs*. 2007;8:113-121.
7. Dworkin RH, Portenoy RK. Pain and its persistence in herpes zoster. *Pain*. 1996;67:241-251.
8. Galer B, Gammaitoni A, Alvarez N. 6. Immunology [XIV.pain]. In: Dale DC, Federman DD, eds. *WebMD Scientific American Medicine*. New York, NY: WebMD Corporation; 2003.
9. Gordon DB, et al. American Pain Society recommendations for improving the quality of acute and cancer pain management. *Arch Intern Med*. 2005;165:1574-1580.
10. Kost R, et al. Postherpetic neuralgia – pathogenesis, treatment, and prevention. *N Engl J Med*. 1996;355:32-42.
11. Merskey H, Bogduk N. Classification of Chronic Pain. 2nd ed. Ann Arbor, Michigan: *IASP Press*; 1994;209-214.
12. Moskowitz MH. Pharmacotherapy of neuropathic low back pain. *Curr Pain Headache Rep*. 2003;7:178-187.
13. Polomano RC, et al. Perspectives on pain management in the 21st century. *Pain Manag Nurs*. 2008;9:S3-10.

