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
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
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
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University of Pennsylvania School of Nursing
Associate Professor of Anesthesiology and Critical Care (Secondary)
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Philadelphia, Pennsylvania

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El Dorado Hills, California

Disclosure Statement
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Consultant: Alpharma Inc.; Baxter Healthcare; Endo Pharmaceuticals; Ortho-McNeil-Janssen Pharmaceuticals, Inc.
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Rosemary Polomano, RN, PhD, FAAN, Chair
About the Faculty

Rosemary C. Polomano, PhD, RN, FAAN, Chair
Associate Professor of Pain Practice
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Associate Professor of Anesthesiology and Critical Care (Secondary)
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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 Scholaristic Academic Achievement. Dr. Polomano has also received national research awards for her investigations related to acute and chronic pain management.
Colleen J. Dunwoody, MS, RN-BC
Advanced Practice Nurse
University of Pittsburgh Medical Center Presbyterian
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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.”
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.

Meeting the Challenges of Managing Patients With Complex Pain Syndromes
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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

Physiology of Pain
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Physiology of Pain Perception

- Transduction
- Perception
- Modulation
- Transmission

- Descending Pathway
- Dorsal Root Ganglion
- Spinal Cord

- C-Fiber
- A-beta Fiber
- A-delta Fiber


Physiology of Pain: Pathways and Effects on Pain Perception

- Pain is a complex process mediated by multiple pathways and mechanisms in both the peripheral and central nervous systems (PNS and CNS [spinal cord and brain]).
- Fundamental characterization of pain
  - Nociceptive/inflammatory
    - Activation of pain-sensitive afferent neural pathways in response to injury
  - Neuropathic
    - Abnormal pain processing due to lesions in the PNS, CNS or both

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
  - Superficial Somatic Pain

Pain syndrome examples
- Traumatic bone fractures
- Muscle sprains
- Post-op incision pain

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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

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 to visceral structures

Pain syndrome examples

- Pancreatitis
- Hepatic Metastases
- Irritable Bowel Syndrome

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


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Prevalence of Neuropathic Pain

Possible Descriptions of Neuropathic Pain

• Sensations
  - Numbness
  - Tingling
  - Hot-burning
  - Paresthetic
  - Paroxysmal
  - Lancinating
  - Electric-like
  - Raw skin
  - Shooting
  - Deep, dull, bone-like ache

• Signs/Symptoms
  - Allodynia: pain from a stimulus that does not normally evoke pain
    - Thermal
    - Mechanical
  - Hyperalgesia: exaggerated response to a normally painful stimulus
    - Muscle and tissue spasm, tightness, and tenderness
    - Muscle weakness and atrophy
    - Skin color changes, rashes, swelling, and temperature abnormality

Nociceptive vs Neuropathic Pain


2. Pancreatitis.
Complex Pain: Definitions

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


Mixed Pain

- Mixed pain includes\textsuperscript{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


Challenges Associated With Mixed Pain

- Delineating the multiple physiological and pathophysiological sources of pain\textsuperscript{1,3}
- Assessing sites and sources of pain through subjective and objective criteria\textsuperscript{1,2}
- Implementing evidence-based multimodal treatment approaches\textsuperscript{1}
- Preventing and managing adverse effects from combination pharmacological therapies\textsuperscript{1,2}
- Knowing when to refer patients to pain management specialists\textsuperscript{3}
- Mixed pain often requires multimodal treatment strategies\textsuperscript{5}

\textsuperscript{3} Crews JC. \textit{JAMA}. 2002; 288:629-632.
\textsuperscript{4} Crews JC. \textit{Am J Manag Care}. 2002;16(Suppl 11):s119-22.
\textsuperscript{5} Crews JC. \textit{Am J Manag Care}. 2002;16(Suppl 11):s119-22.
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)

Possible Nociceptive vs Neuropathic Components of LBP

Nociceptive Pain: Caused by activity in neural pathways in response to potentially tissue-damaging stimuli.

Mixed Type: Caused by a combination of both primary injury and secondary effects.

Neuropathic Pain: Initiated or caused by primary lesion or dysfunction in the nervous system.

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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**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

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

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 therapy3,4
   - Considerations
     - Past history of drug or alcohol abuse
     - Low starting dose
     - Dosing spread around the clock and not prn

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


Clinical Case: CLBP

Is the answer…?

c. Worsening depression
  - Pain may be a sign of depression

Is Depression Worsening? LBP ↔ Psychological Factors

- Prolonged back pain may be associated with a psychological disturbance, manifesting as:1-3:
  - 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

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


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

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 pain
- Opioid “tolerance” may not be a downregulation of analgesic systems, but an upregulation of hyperalgesic systems

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Differentiating OIH From Other Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Nature of Pain</th>
<th>Presentation or Onset of Pain</th>
<th>Response to Opioid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid-induced hyperalgesia</td>
<td>Increased sensitivity to pain; diffuse pain, extending beyond the distribution of pre-existing pain; allodynia may be present</td>
<td>Abrupt onset with rapid opioid escalation or high-dose opioid administration</td>
<td>Pain worsens</td>
</tr>
<tr>
<td>Worsening pain pathology</td>
<td>Localized to site of pre-existing pain or new site of pathology</td>
<td>Variable, depending on source of pain</td>
<td>Pain improves</td>
</tr>
<tr>
<td>Opioid tolerance</td>
<td>Localized to site of pre-existing pain</td>
<td>Gradual onset</td>
<td>Pain improves</td>
</tr>
<tr>
<td>Opioid withdrawal</td>
<td>Increased sensitivity to pain; diffuse, extending beyond the distribution of pre-existing pain</td>
<td>Abrupt with short-acting opioid or antagonist administration; gradual with long-acting opioids</td>
<td>Pain improves</td>
</tr>
<tr>
<td>Opioid-addictive disease</td>
<td>Increased sensitivity to pain; diffuse, extending beyond the distribution of pre-existing pain</td>
<td>Gradual onset</td>
<td>Pain may improve but functionality may worsen</td>
</tr>
<tr>
<td>Pseudoaddiction</td>
<td>Localized to site or pre-existing pain</td>
<td>Variable, depending on source of pain</td>
<td>Pain improves</td>
</tr>
</tbody>
</table>

Table adapted from Compton 2008 and Mitra 2008.


Differential Assessment

- General principles
  - Presence of worsening pathology or psychological influences can contribute to reports of increased pain, but are not related to opioid administration
  - Tolerance, withdrawal-related symptoms, pseudoaddiction, or addiction can be differentiated by increasing opioid dose and/or frequency
  - If reports of pain increase with upward opioid titration, OIH should be considered

Clinical Case: CLBP

Or is the answer…?
e. Aberrant drug-seeking behavior
  - Behavior outside of the socially accepted norm
  - Multiple dose escalations

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Should Aberrant Behaviors and Substance Abuse Be Considered?

- Occurrences of substance abuse or addiction with chronic opioid therapy remain unknown
- Health professionals don’t always agree on what constitutes aberrant drug behaviors
- Data suggest patients receiving chronic opioids engage in at least 1 noncompliant behavior
- Risks include combinations of psychosocial, drug choice and genetics
- Concerns regarding tolerance and physical dependence should not be linked to substance abuse

Drug-related Behaviors That Need to Be Evaluated

<table>
<thead>
<tr>
<th>Probably less predictive</th>
<th>Probably more predictive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aggressive complaining</td>
<td>Selling prescription medications</td>
</tr>
<tr>
<td>Medication hoarding when symptoms are milder</td>
<td>Prescription forgery</td>
</tr>
<tr>
<td>Requesting specific medications</td>
<td>Stealing or “borrowing” medications from another person</td>
</tr>
<tr>
<td>Acquisition of medications from other medical sources</td>
<td>Injecting oral formulation</td>
</tr>
<tr>
<td>Unsanctioned dose escalation once or twice</td>
<td>Obtaining prescription medications from nonmedical source</td>
</tr>
<tr>
<td>Unapproved use of the medication to treat another symptom</td>
<td>Multiple episodes of prescription “loss”</td>
</tr>
<tr>
<td>Reporting psychic effects not intended by the clinician</td>
<td>Concurrent abuse of related illicit drugs</td>
</tr>
<tr>
<td>Occasional impairment</td>
<td>Multiple dose escalations despite warnings</td>
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Treatment Strategies for LBP

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Possible Cause of LBP</th>
<th>Treatment Strategies</th>
</tr>
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<tbody>
<tr>
<td>Intermittent unilateral leg pain, numbness, weakness radiating to foot</td>
<td>Intermittent nerve entrapment with nerve root inflammation</td>
<td>Short-acting opioids</td>
</tr>
<tr>
<td>Constant burning, stabbing, or deep aching groin or leg pain</td>
<td>Permanent nerve damage</td>
<td>Nonsteroidal anti-inflammatory drugs (NSAIDs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Topical analgesics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioids</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tricyclic antidepressants (TCAs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anticonvulsants</td>
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Treatment Strategies for LBP

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<tr>
<td>Axial, aching, throbbing, and/or stabbing LBP with trigger points radiating to buttocks and anterior thigh</td>
<td>Inflammation of surrounding tissue or joint, myofascial</td>
<td>NSAIDs, Opioids, Topical analgesics</td>
</tr>
<tr>
<td>Pain &gt; expected from injury, burning, electrical, to one or both limbs, edema, motling, nail, skin, and hair changes, temperature change, allodynia, hyperalgesia</td>
<td>Sympathetically maintained pain</td>
<td>Opioids, TCAs, Anticonvulsants, Topical analgesics</td>
</tr>
</tbody>
</table>


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


Tapentadol ER: Effective in CLBP

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

![Graph showing pain intensity comparison between Tapentadol ER, Oxycodone CR, and Placebo]

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### Tapentadol ER: Improved Tolerability

<table>
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<tr>
<th>Incidence of Treatment-emergent Events for Tapentadol ER and Oxycodone CR</th>
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<tbody>
<tr>
<td>Event</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Disgust</td>
</tr>
<tr>
<td>Somnolence</td>
</tr>
</tbody>
</table>


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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

- **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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Tapentadol ER: Effective in CLBP

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

Tapentadol ER Oxycodone CR Placebo

-4.9 -4.9 -4.1


Tapentadol ER: Improved Tolerability

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

Nausea Vomiting Constipation Dizziness Somnolence

Tapentadol ER Oxycodone CR


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
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  - Schedule physical therapy

Schematic of Varicella Zoster Virus (VZV) Latency and Reactivation

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

HZ = Herpes Zoster

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

Chronic Pain From PHN

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

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Typical Locations of Herpes Zoster

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

Characterization of Pain Associated With PHN

- Dysesthesia: an unpleasant abnormal sensation, spontaneous or evoked\(^1\)
- Hyperalgesia: pain of exaggerated severity in response to normally painful stimulation\(^1\)
- Allodynia: pain evoked by a normally innocuous stimulus\(^1\)
  - 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 CNS\(^2\)

PHN: Risk Factors

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

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Duration of Pain Associated With PHN and Increased Age

- Patients reporting pain (%)*
  - >1 year
  - 6-12 months
  - 1-6 months
  - <1 month


Evaluating Outcomes With PHN

- Worst pain intensity levels moderate to severe
- Pain caused measurable interference with general activity (40%), mood (45%), and enjoyment of life (48%)
- 31% had relatively low levels of satisfaction with pain medication
- 44% moderate anxiety and depression
- Brief Pain Inventory (BPI) utilized to evaluate pain in recent herpes zoster vaccine trial


Pain Intensity With PHN

- Average pain
- Worst pain
- Least pain
- Current pain

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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
  - 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

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)

Management Strategies for PHN

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine 5% patch</td>
<td>Erythema or rash</td>
</tr>
<tr>
<td></td>
<td>Caution in patients receiving class I antiarrhythmics</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Anticholinergic AEs, sedation, cardiac conduction abnormalities</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Somnolence, dizziness, gait disturbances, gastrointestinal (GI) upset</td>
</tr>
<tr>
<td>Opioid analogues</td>
<td>CNS- and GI-related AEs</td>
</tr>
<tr>
<td>Dual-mechanism agents</td>
<td>Similar to opioids but with better GI profile</td>
</tr>
</tbody>
</table>

AEs = adverse effects

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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

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)**

Management of PHN


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

Topical vs Transdermal Medication Delivery Systems

<table>
<thead>
<tr>
<th>Topical (lidocaine patch 5%)</th>
<th>Transdermal (fentanyl patch)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral tissue activity</td>
<td>Systemic activity</td>
</tr>
<tr>
<td>Applied directly over painful site</td>
<td>Applied away from painful site</td>
</tr>
<tr>
<td>Minimal systemic absorption</td>
<td>Serum levels necessary</td>
</tr>
<tr>
<td>Systemic AEs rare</td>
<td>Systemic AEs common</td>
</tr>
</tbody>
</table>


Lidocaine Patch 5%

- Lidocaine 5% in pliable patch
- Up to 3 patches applied once daily directly over painful site
  - 12 h on, 12 h off (FDA-approved label)
  - Published data indicate 4 patches (18-24 h) safe
- Efficacy demonstrated in 3 randomized controlled trials on PHN
- Drug interactions and systemic adverse effects unlikely
  - Most common adverse effect: application-site sensitivity
- Clinically insignificant serum lidocaine levels
  - Mechanical barrier decreases allodynia

1. Lidoderm (lidocaine patch 5%) [package insert].

Classes of Pain Medications: Antidepressants

- Tricyclics: Examples: amitriptyline, nortriptyline, desipramine
  - Inhibit both norepinephrine (NE) and serotonin reuptake to varying degrees
  - Possess other properties (eg, local anesthetic-like activity)
- Serotonin norepinephrine reuptake inhibitors (SNRIs): Examples: venlafaxine, duloxetine, bupropion
  - Selective serotonin reuptake inhibitors (SSRIs) have not been shown to be particularly effective in pain therapy
  - Adverse effects vary by class of agent, and include dry mouth, blurred vision, nausea, constipation, agitation, dizziness, and drowsiness

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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

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

![A Comparison of Pain Intensity Reduction with 3 Antidepressants](chart.png)

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
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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

<table>
<thead>
<tr>
<th>Week</th>
<th>Placebo (N=116)</th>
<th>Gabapentin (n=109)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-0.2</td>
<td>-0.3</td>
</tr>
<tr>
<td></td>
<td>-1.0</td>
<td>-2.0*</td>
</tr>
<tr>
<td></td>
<td>-1.6*</td>
<td>-2.1*</td>
</tr>
</tbody>
</table>

**Change From Baseline in Average Daily Pain Score**


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

**Mean Weekly Visual Analog Scale Scores Comparing Oxycodone to a Placebo**


Managing Complex Pain Syndromes

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

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 Society
    - American Society of Regional Anesthesia and Pain
    - American Society of Anesthesiology

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Practice Guidelines for Chronic Pain Management

- Chronic pain therapy1:
  - History and physical examination
  - Diagnostic evaluation
  - Counseling and coordination of care
  - Monitoring and measurement of clinical outcomes
  - Multidisciplinary pain management2
  - Multimodality pain management
  - Adjuvant pharmacological interventions


The Complexity of Pain

- Multimodal therapy provides a way to achieve balanced, safer pain therapy2
  - Improved quality of analgesia
  - Fewer adverse effects
  - Better functional status3
- Distinct from polypharmacy

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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 NE
  - Available in Immediate Release (IR) formulation
  - Clinical trial experience
    - Comparable to oxycodone in acute pain (bunionectomy) and in more chronic pain (up to 90 days in joint or back pain)
    - Comparable or better pain relief than morphine in dental surgery
    - Main adverse effects similar to conventional opioids (GI, CNS), but significantly better GI profile, including lower rate of constipation
  - May be associated with less tolerance
- May be useful in patients with opioid sensitivity

- Tapentadol ER: emerging extended-release formulation
  - Acts on mu opioid receptors and inhibits reuptake of NE
  - Demonstrate efficacy and safety in:
    - Moderate to severe chronic pain due to osteoarthritis of the knee
    - Chronic low back pain. Comparable with oxycodone in pain intensity relief with improved GI tolerability
  - Management of chronic neuropathic pain in patients with diabetic peripheral neuropathy
  - Better gastrointestinal tolerability compared with oxycodone

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

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### 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\(^1\),\(^2\),\(^3\),\(^4\)
  - Mechanisms of action and pharmacodynamics
  - Synergistic and AEs
  - Ensure timely administration of all analgesics, avoiding gaps in analgesia\(^2\)–\(^4\)
  - 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\(^1\),\(^2\),\(^4\)


### 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

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Suggested Reading List


